University of Khartoum

The Graduate College

Medical & Health Studies Board

INTRANATAL AND EARLY NEONATAL OUTCOME OF MULTIPLE-BIRTH NEWBORNS IN SOME HOSPITALS IN KHARTOUM STATE

BY

DR. BABIKER HAMID MOHAMMAD

MBBS (U of K) 1998

A thesis submitted in partial fulfillment for the requirement of the

Clinical MD in Paediatrics and Child Health

Supervisor

DR. YAHIA SHAKIR ABDEL GADIR

MBBS (U of K), MPCH (U of K)

Associate Professor

Department of Paediatrics & Child Health,

Faculty of Medicine, U. of Khartoum.

2005

Contents

قال تعالى :

(هل أتي علي الانسان حين من الدهر لم يكن شيئا مذكورا (1) انا خلقنا الانسان من نطفة أمشاج نبتليه فجعلناه سميعا بصيرا (2).

صدق الله العظيم

سورة الأنسان

Dedication

To

My dear parents . . .

My Teachers. . .

My Fiancee, Rehab . . .

My sisters & brothers . . .
&

All children in the world . . .

Babiker

ACKNOWLEDGMENT

This study was done with much assistance from my supervisor Dr. Yahia Shakir Abdel Gadir , so grateful to him for his substantial input. I am particularly indebted to his patience; advices and encouragement. I have had generous help from colleagues, sisters and the statistician Mr. Hassan Ali. Again I am indebted to them.

Also I acknowledge Mr. Khalid, who had printed this book, the mothers who gave me the consent and to all multiple-birth newborns in my favourite country, Sudan.

ABSTRACT

This study was done to determine intranatal outcome and maternal risk factors of multiple- birth newborns .The study was a prospective, case-control hospital-based, conducted in Omdurman Maternity Hospital, Khartoum Teaching Hospital, and Khartoum North Teaching Hospital, between July and December 2004. During this interval of time, 222 babies were delivered (70 were twin pairs (140), 3 were sets of triplets (9) and 73 were singletons as control).

146 mothers were enrolled in this study (73 of them had given birth to twins or triplets and 73 had given birth to singletons '' control'').

Increased parity, positive family history of multiple pregnancy and advanced maternal age were the risk factors for multiple pregnancies.

Pre-term births, low-birth weights and asphyxia were the major complications associated multiple pregnancies .The mortality rate of multiple- birth newborns was 134.2/1000 and that of singletons was 13.6/1000.

Maternal counseling about the effect of increased parity and age on the multiple pregnancies will lead to decrease in the incidence of multiple pregnancies.

Prevention of pre-term deliveries in multiple birth pregnancies, prompt application of knowledge of neonatal resuscitation achieved by attendance of multiple- birth deliveries by paediatric registrars, will lead to the more optimistic of us to expect the dramatic decrease in intranatal and early neonatal mortality, morbidity, and future handicaps.

مستخلص الأطروحـــــــة

هذه الدراسة أجريت لتحديد مصير الرضع في الفترة التي تتعلق بزمن الولادة ولتحديد الأسباب المساعدة على الولادة المتعددة في بعض مستشفيات ولاية الخرطوم ، في الفترة ما بين يوليو وديسمبر من عام أربع وألفين للميلاد. خلال هذه الفترة الزمنية تمت ولادة 222 طفل منهم 70 توائم 140 "طفل "، 3 ولادات ثلاثية الإنجاب 9 "أطفال " و 73 طفل آخرون للمقارنة. (أيضا تم استجواب 146 أم 73 منهن أنجبن أطفال متعددي الولادة و 73 منهن أنجبن أطفال أحادى الولادة أخذن للمقارنة)

ازدياد إنجابية الأمهات ، وجود الحمل المتعدد في العائلة وتقدم الأمهات في السن ، كانت هي العوامل المساعدة على حدوث الحمل المتعدد .

الولادة المبتسرة قبل التاريخ المحدد لها ، (أوزان الرضع الناقصة والاختناق ، كانت هي المضاعفات الأساسية المصاحبة للولادة المتعددة).

معدل وفيات الرضع متعددي الولادة كانت 132.2/1000، بينما معدل وفيات الرضع أحادى الولادة كانت 13.6/1000.

إرشادات الأمهات بتأثير تعدد الولادات والتقدم في السن على معدل حدوث الحمل المتعدد، سيؤدى إلى انخفاض معدل حدوث هذا النوع من الحمل .

منع الولادة المبتسرة في حالة المتعدد والتطبيق الجاد للمعرفة في إسعاف حديثي الولادة ، والذي يتمك بحضور نواب الأطفال لمثل هذا النوع من الولادات ، سوف يجعلنا أكثر تفاؤلاً بتوقع انخفاض هائل في كل مرض ومعدل وفيات حديثي الولادة والإعاقة المستقبلية .

ABBREVIATIONS

C/S:	Cesarean Section
CNS:	Central Nervous System
CP:	Cerebral Palsy
CXR:	Chest X–Ray
DZ:	Dizygotic
ELBW:	Extreme Low-Birth Weight
FFFTTS:	Feto – Feto -Fetal Triple Transfusion Syndrome
FFTS:	Feto –Fetal –Transfusion Syndrome
HMD:	Hyaline Membrane Disease
IUFD:	Intrauterine Fetal Death
IUGR:	Intra Uterine Growth Retardation
IVF:	Invitro Fertilization
IVH:	Intraventricular Hemorrhage
LBW:	Low– Birth Weigh
LITT	Lazer Induced Thermotherapy
LTOC:	Largngotracheoesophageal Cleft
MZ:	Monozygotic
NBS:	New Ballards Score
NEC:	Necrotizing Enterocolitis
NICU:	Neonatal Intensive Care Unit
PNM:	Perinatal Mortality
RDS:	Respiratory Distress Syndrome
SGA:	Small For Gestational Age

SIDS:	Sudden Infant Death Syndrome
UPH:	Unilateral Pulmonary Hypoplasia
WHO:	World Health Organization

List of Table

List of Figures

Page

1- INTRODUCTION AND LITERATURE REVIEW

1.1 Background:

Multiple gestations are the conception of more than one fetus, and result from ovulation and subsequent fertilization of more than one Oocyte. In such cases the fetuses are genetically different (binocular, dizygotic or non-identical). Multiple gestations can also result from splitting of one ovum (monozygotic or uniovular) [1].

When the single embryonic mass splits into two within three days of fertilization , the fetuses are diamniotic . When splitting occurs after the 3rd day of fertilization, there is a vascular communication (monochorionic). Embryonic splitting after the 9th day following fertilization results in monoamniotic monochorionic twins, and splitting after the 12th day results in conjoined twins [1].

Dizygotic twins have their own amniotic sac(diamniotic), and placentas (dichorionic). In all diazygotic pregnancies

there are two separate placentas. In two- third of monozygotic pregnancies, there is a vascular communication within the two placentas (monochorionic), and in one third of cases there are dichorionic placentas . In monozygotic twins , there may be a sharing of the same placenta (monochorionic), amniotic sac (monoamniotic) or even fetal organs (conjoined or siamese). Chorionicity rather than zygosity is associated with greater fetal risks.[1]

Triplets can be monozygotic , dizygotic or trizygotic.

Trizygotic triplets occur when 3 sperms fertilize 3 ova. Dizygotic triplets develop from one set of monozygotic co-triplets and a third co- triplet derived from a different zygote [2].

Determination of zygosity and chorionicity:

Zygosity can only be determined by DNA finger-printing , but extensive examination of blood group , red cell enzymes and histocompatibility antigens are widely used methods of genotyping and these methods have only 3% chance of misclassifying dizygotic as monozygotic twins. Indeed these tests are only done for newborns of the same sex.

Prenatally, such tests require an invasive procedures

to sample amniotic fluid (amniocentesis), placental tissue (chorionic villous sampling), or fetal blood (cordocentesis). Chorionicity can be determined by ultrasound, and relies on the assessment of fetal gender, number of placentas and characteristics of the membrane between the two-amniotic sacs. Different sex twins are dizygotic (DZ), and therefore dichorionic, but in two third of twins pregnancies , the fetuses are of the same sex and these are either being monozygotic (MZ)or (DZ) twins [(1).]

Similarly, if there are two separate placentas, the pregnancy is dichorionic, but in the majority of cases the placentas are adjacent to one another and there are often difficulties in distinguishing between dichorionic-fused and monochorionic placentas. In dichorionic twins, the intertwines membrane is composed of the central layer of chorionic tissues sandwiched between layers of amnion, whereas in monochorionic twining there is no layer consequently the intertwins membrane is thicker and more echogenic in dichorionic than in monochorionic twins [(2).]

1.2 Epidemiology and Risk Factors:

The incidence of multiple pregnancy is 1% of all pregnancies, with 2/3 being DZ and 1/3 being MZ. This incidence varies with the following risk factors:-

1.2.1 Ethnic group:

Multiple pregnancy is influenced by the race .

Up to 5 times higher in certain parts of Africa, and half as high in parts of Asia [1].

In USA the overall prevalence of twins is 12 per 1000. The birth rate of DZ twining is highest among African Americans (10-40/1000 births), followed by Caucasians (7-10/1000 births), and Asian Americans (3/1000 births)[3].

In an epidemiologic study done in USA , multiple birth rate among whites and blacks was assessed, it was found to be increasing more rapidly among whites than among blacks.[4]

Other specific rates of incidence include:

Belgium 1:56 ; Italy 1:86 ; American white , 1: 82 ; Greece , 1: 1300.

In United States of America the overall incidence of twins is 2-5:100, of triplets is 1:7400, and in quadruplets is

1:640000 [5].

1.2.2 Parity:

Females with a higher parity have a higher chance of multiple pregnancy than those with lower parity [1].

Rising maternal parity was found to be a strong risk factor for multiple pregnancy in a Nigerian study . In this study they found that the parity range was 0-14 year with a mean of 28 ± 5.4 years [6].

The same relationship was also found in Ghana in a case-control study compared twins and singletons. [7].

A study was done in Maltese Islands to analyze the multiple birth statistics since 1959. Hospital twin birth deliveries during the period of 1983 – 1985 were analyzed for numbers of variables. The incidence of multiple pregnancy for the Maltese islands appeared to be decreased slightly since 1958 with an over all rate of 10.21 per 1000 maternity . The ratio of DZ to MZ twining was 1.64. Patients with multiple pregnancy are shown to be elderly and multiparous. The newborn infants are likely to be premature and of low birth weights, and their perinatal mortality rate is markedly in

excess of that of singletons [8].

1.2.3 Maternal age:

Multiple pregnancy is strongly linked to maternal age (the older the lady the greater is the chance to have multiple pregnancy) [1].

In Ghana , a retrospective study involving 623 twins , and 1246 singleton births was done to compare the 2 groups with regard to selected maternal and fetal characteristics and outcome . They found that maternal age was significantly higher for those who had become pregnant with twins [7].

A study done in Nigeria between 1992 and 1998 to analyze epidemiological variables incidence and perinatal and maternal outcome of twin pregnancy . They found that the incidence of twin pregnancy was 28/1000, triplets was 0.4/1000 and quadruplets was 0.07/1000. The age range of the twin mothers was 15-47 years. They concluded that rising maternal age is significantly associated with twining rate [6].

In USA a retrospective study (using vital statistics data from the National Center for Health Statistics) was done to describe changes in the epidemiology of multiple births from

1980 to 1999 by race , maternal age and region . The overall multiple births ratio increase was 59% (from 19.3 to 30.7 multiple births per 1000 live births , p <0.001). Women of advanced maternal age , especially those aged 30-34 years , 35-39 years , and 40-44 years , experienced the greatest increases (62% , 81% and 110% respectively) [4].

A study done to evaluate the impact of maternal age and use of fertility drugs on multiple birth prevalence from 1970 to 1995 in the Netherlands. A population-based survey was carried out in which data were collected from the Central Bureau voor Statistiek, the Institute of Medical Statistics and from all clinics for in vitro fertilization. It was found that in the last two decades, the prevalence of multiple births, especially of twin and triplet births, has increased significantly. Three possible explanations for this phenomenon are: (1) introduction of assisted reproductive techniques in combination with fertility drugs; (2) increasing maternal age; and (3) decreasing fecundity with increasing maternal age, resulting in more fertility treatments. A surplus of 1,366 twins was born in 1995 as compared to 1975. The expected excess of

twins was 1,368, of which 104 (7.6%) were a result of the increase in *total* births in 1995, 583 (42.6%) were due to maternal age > 29 years, and, respectively, 330 (24.1%) and 351 (25.7%) twins were due to in vitro fertilization treatment and intrauterine insemination. It was concluded that the delay in achieving pregnancy and the use of fertility-promoting therapies profoundly affect the prevalence of multiple pregnancies in a given country. The general population should be informed of this risk. [9]

A study done in Japan to estimate zygosity of triplet births. Increased maternal age was found to be linked with increased trizygotic triple rates [10].

Twining rates from the years 1975 up to 1979 in Catalonia (Spain) are presented. Crude rate are very low (7.62 per 1000 maternity). The DZ twining rate and MZ twining rate were 3.74 and 3.88 respectively. Sex ratio among twin couples is very low (0.49 male Vs 0.51 female births).

A multiple linear stepwise regression on the twining rates shows MZ rates to be influenced by order and father's age and DZ rates by mother's age [11].

1.2.4 Method of conception:

The use of hormonal treatment and assisted reproductive techniques for infertile women was found to be a major risk factor for multiple gestation [1].

Although the incidence of spontaneous multi-fetal gestation remains stable, the overall incidence is increased dramatically over the past 10-15 years in many developed countries of the word . Data from England and Wales showed that between 1980 and 1993 the twins maternity rate increased by approximately twenty-five percent , the triplet and higher order maternity rate is more than double . Similar trends have been reported elsewhere . The majority of these increases have been linked to the use of ovarian stimulants and assisted reproductive techniques , and multiple pregnancy must be considered as one of the most important adverse outcome of current methods of infertility treatment . The prevalence of twining and higher order multiple births is increasing in USA and elsewhere , due to at least in part to fertility- enhancing medical therapies [12-18].

In Japan zygosity of triplet births was estimated, during

the period from 1975 to 1994 . The DZ triplets rate was increasing , MZ triplets rate remained constant , while trizygotic triplets was also increasing . This increase in trizygotic triplets rate was attributed to ovulation-inducing hormones [10].

In Netherlands a study to evaluate the impact of fertility drugs on multiple births prevalence from 1970 to 1996 was done. They found that the prevalence rate of twins and triplet is increased[19].

Neonatal outcome was studied after ovarian stimulation to 4029 women who delivered between 1995-1999 and compared to 438.582 women who did not had ovarian stimulation . It was found that the twining rate was 5.9% in the study group and 1.2% in the control group , the triplet rate was 0.5% in the study group and 0.02% in the control group [20].

A study done to examine trends in multiple births conceived using assisted reproductive technology (ART) in the United States between 1997 and 2000 and to estimate the proportion of all US multiple births attributable to ART use. A

population-based data of 109 519 live-born infants who were conceived in the United States using ART and born between 1997 and 2000 and population-based data of 15 856 809 live-born infants who were delivered in the United States between 1997 and 2000 was analyzed. Multiple birth rates (the number of live-born infants delivered in multiple gestation pregnancies per 1000 live births) and the proportion of all US multiple births attributable to ART were evaluated. The twin rate for ART patients increased between 1997 and 2000, reaching 444.7 per 1000 live births in 2000, whereas the triplet/+ rate declined substantially from 134.3 to 98.7 per 1000 live births from 1997-2000. From 1997-2000, the proportion of multiple births in the United States attributable to ART increased from 11.2% to 13.6%, whereas the proportion attributable to natural conception decreased from 69.9% to 64.5%. In 2000, the proportion of triplet/+ births attributable to ART and to natural conception was 42.5% and 17.7%, respectively. The contribution of ART to multiple births increased substantially with maternal age, from 11.6% for triplet/+ infants born to women aged 20 to 24 to 92.8% for women aged 45 to 49 years.

It was concluded that the contribution of ART to twin birth rates continues to increase, but the contribution of ART to triplet/+ birth rates has declined. [21]

1.2.5 Twining in families:

Among the risk factors for natural multifetal pregnancy, family history of dizygotic twins is an important one[22].

Risk factors for multiple gestation include assisted reproduction techniques (both ovulation induction and in-vitro fertilization or IVF), increasing maternal age, high parity, black race and maternal family history [23].

A study was conducted in Netherlands, on twining in relative of consecutive triplet sets in Aland Island. The incidence of twining in sibships of triplets was extremely high, 80/1000 (56/1000 before and 143/1000after the triplet maternity) . In Finland as a whole, 1905-1954, the twining rate among mothers of triplets was 38/1000, i.e. 2.6 times the rate in general population. In the sibships of triplets, there was a low rate of twining (below 10/1000), both of the same

sex (SS) and opposite sex (OS). Triplets among mothers' sibships of OS triplet the twining rate was 18/1000, and among mothers sibships of SS triplets was 26/1000. The series of triplet families from both Land and Finland indicate a considerably higher frequency of twining on the maternal than on paternal side. In sibships of triplets not only the DZ but also the MZ twining rates were approximately twice as those in the general population. The triplet rate in Finland is strongly increasing with maternal age and was in the last century among mother of 30- 39 years of age considerably higher than among mothers from this century. Mothers of triplet in Finland had a high frequency (more than 40 %) of preoptically conceived the first born .This indicates that they conceive with greater ease and for many have better physical condition than other women for completing a gestation with multiple embryos[24].

An excess of twins in families with the Martin-Bell or fragile (x) syndrome was noted previously in one family study [Ftyns, 1986] . A study was done to confirm this observation in a second large sample of families from a different

population. The number of twins is calculated among the total number of live birth of known obligate carriers for fragile (x) families ascertained in New South Wales, Australia. There were 5 male pairs, 3 female pairs and 9 unlike sex pairs of twins born among 752 live births. Thus the twining rate was 1/44 per live birth. The rate is compared to that found in 2 different types of individuals : 1) the rate of 1/96 which was obtained from the 1985 vital statistics for New South Wales , and 2) the rate 1/75 obtained from a sample of live births of obligate carriers with haemophia A. The increase in twining among heterozygotes with fragile (x) was highly significant when compared to the census data ($P < 0.001$). However, it was not significantly different from that in the hemophilia A data ($P < 0.05$) which were collected in the same way as in the fragile (x) families [25].

1.2.6. Studies in Sudan:

The 1st study was done by Dr N. Elsadig at 1997 to estimate the incidence of twin pregnancies and to asses the effect of demographic and socioeconomic factors, and intercurrent medical history in the outcome of such

pregnancies in Soba Hospital. 71 (2.8% of total delivery) consecutive twin pregnancies were compared with the same number of randomly chosen singleton deliveries following spontaneous conception . DZ were in excess of MZ. More twin pregnancies found among multiparous patient (74.65%) with low socioeconomic status . Family history was found a strong determinant of incidence (61%) . Maternal age was found to be parallel with that of general obstetric population (20-30 years).

Intercurrent medical diseases and pregnancy complications were more common among twin pregnancies than singleton pregnancies (83.09%Vs 54.92%) . Higher rate of preterm , low birth weight , malpresentation of the second twins accounted mainly for the higher perinatal mortality rate, which was 77.5 per 1000 birth in the second twins versus 42.25 per 1000 in the first [26].

Primary cesarean section for malpresentation was found to have a slightly better effect on the perinatal outcome . She concluded that twin pregnancies are at high risk and benefit from early diagnosis , prevention and treatment of term birth and the quantity of antenatal care will provide better results.

The second study was carried out by Dr I. A. Adam on 1998 to find out the outcome of twin deliveries and perinatal mortality of the second twin compared with that of the first twin , among patient who delivered at Omdurman New Hospital and Elsheikh Ali Fadul Hospital .

In this study there were 74 twins delivery (148 births) , of these there were 12 still births and 3 early neonatal deaths with overall mortality rate of 101.4/1000. The perinatal labour and LBW were the main causes of perinatal mortality .

Perinatal mortality of the second was higher than that of the first due to prolonged enter-twin interval. The study recommended the importance of diagnosis and adoption of active management in the delivery of the second twin. It also recommended C/S if the first twin is presenting other than cephalic [27].

Ibrahim S. (1994) conducted a cohort study of risk factors of intranatal mortality, to determine perinatal and late neonatal mortality in the rural community in Sudan. A total of 13060 deliveries were monitored over 6 years period (from 1985 to 1991). The risk of an unfavourable outcome (stillbirth

or neonatal death) in multiple pregnancies was more than nine fold that of singleton ones. Among twins who survived the neonatal period, 17 (37 %) were first born, and 9 (20 %) were second born twins [28].

Yousif G. (1996) [29], studied 254 patients by a retrospective, case-control study at Soba University Hospital. He found that the incidence of preterm births was 4.92%, and prematurity is directly related to multiparity, history of previous preterm deliveries, and multiple pregnancies[29].

Salwa A. Gadalla conducted a study in Omdurman Maternity Hospital to assess the factors associated with low birth weight from 28th April to 27th may 2001. Atotal number of 300 birth were assessed. She found that multiple pregnancy is strongly associated with low birth weight (85% of twins were of low birth weight { P. <0.001}). [30]

Another study was done by Nawal Mahmoud Ahmed , for the application of risk approach in maternal and child health care in Sudan. She found that multiple pregnancy among the other factor is strongly associated with neonatal problems. Specifically prematurity and birth trauma. [31]

1.3 Complications of multiple pregnancies:

With the decline in prenatal mortality and morbidity from other causes , multiple pregnancy now warrants special attention since it increases in incidence and make disproportionate contribution to prenatal mortality and morbidity in excess of that due to multiplication of singletons risk by fetal numbers . Recognizing the specialized nature of multiple pregnancy management, the Royal College of Obstetric and Gynaecology recommended that multiple pregnancy must be managed by a single consultant team within any one hospital (Ward and Whittle 1995) [32].

Again every maternal risk, like polyhydramnios, antipartum hemorrhage, postpartum hemorrhage, gestational diabetes, pregnancy- induced hypertension, maternal death …. etc , occurs more frequently , which might adversely affect the fetus(s) and /or the newborn infant(s) . These risk factor are mainly attributed to preterm labour and prematurity , but others like delayed inter-twin interval , malpresentation, birth injury , and congenital malformations can also affect the

fetus and the newborn. Fortunately during the past 3 decades prompt application of new knowledge of practical pathophysiology has dramatically improved the quality of the surviving tiny premature infants , the result of prompt correction, and if possible, prevention of such interrelated insults such as hypoglycaemia, asphyxia, hypoxia, jaundice and shock , have made us to expect the virtual disappearance of neurological problems, previously considered the unavoidable legacy of the surviving premature infant [33].

1.3.1 Intrauterine Fetal Death (IUFD):

IUFD of one fetus in a twin pregnancy may be associated with a poor outcome for the co-twins but the type and degree of risk depends on the chorionicity, the monochorionic twining being more liable to severe risk . Second or third trimester IUFD of one fetus may be associated with the onset of labour in dichorionic twins, and acute hypotensive episodes in monochorionic twins leading to handicap of the co-twins in 25% of cases . The mechanism is acute haemodynamic shift from the alive to the dead fetus.

Perinatal mortality rate : The number of live –born infants who die under the age of 28 days per 1000 live birth in the same year. Neonatal deaths are also divided in to those occurring during the first week of life (early neonatal deaths) and those from 8-27 days of age (late neonatal deaths) .

Still birth : a child born after the 28th week gestation , which after being expelled from the mother does not breathe or show other signs of life such as heart beat , umbilical pulsation or movement of muscles (34).

The late fetal-early neonatal period is the time of life with the highest mortality rate of any age interval . Perinatal mortality refers to fetal deaths occurring from the twentieth week of gestation , until the seventh day after birth , and is expressed as a number of deaths per 1000 live birth . IUFD represents 40-50 % of PNM rate , such infants are defined as stillborns (35).

Perinatal mortality rate in twins is 5 times higher , and in triplets is ten times higher than that of singletons(32).

The dynamics of perinatal mortality rates (PNMR) and

causes of death in twin pregnancies over 13 year in the Northern Region of the National Health Service in England is described . All twin perinatal deaths occurring between 1982 - 1994 were identified from the Northern Region Perinatal Mortality Survey. The twinning rate increased from 9.9 per 1000 maternities in 1982 to 12.0 per 1000 in 1994. There was a total of 10.734 twin pregnancies and these 421 resulted in 530 perinatal deaths. The perinatal mortality rate in twins is significantly decreased over time (1982 -87 ,55.4 per 1000 ; 1988 -94 , 44.4 per 1000 ; p=0.01) [36].

Twins with very low birthweight (< 1500g) comprised 69% , and preterm twins (< 37completed weeks of gestation) comprised 74.9 % of all twin perinatal deaths . The major immediate cause of early neonatal death was pulmonary immaturity (63%), and antepartum anoxia caused 76.9% of antenatal deaths. Unexplained preterm labour and intrauterine death were the leading obstetric factors underlying death in twins. Despite a decrease over the 13 years, the perinatal mortality (PNM) rate in twins in the Northern Region remains high [36].

PNM rate are reported from 146 twin-1 and 192 twin-2 among 622 consecutive twin pairs delivered at University of llorin Teaching Hospital , llorin ,Nigeria . Stillbirth and infants with severe birth asphyxia (Apgar score 1-3) were recorded in a significant proportion for both 1st and 2nd twins . PNM rate is 13.7 in twin-1, 18.8in twin-2 ; corrected PNM for infants weighing 2kg or more , were 9.3 and 12.4 for twin-1 and twin-2 respectively . Factors such as LBW , malpresentation , retained second breech, contribute significantly to the higher PNM rate [37].

A paper reports on 9 twin pregnancies in the years 1982-87 with intrauterine death of single fetus in West Germany was done. The incidence of ten is consistent with that reported in other comparable studies. Evaluation of the causes of death showed a preponderance of asphyxia . Fetofetal transfusion syndrome occurred in four cases. Eight of pregnancies were terminated by C/S . On the basis of this and other experiences described in the literature, some general guidelines are proposed for the management of further pregnancy and delivery in such risk cases[38].

A study was done to describe changes in the epidemiology of multiple birth in USA from 1980 to1999 by maternal factor , and to examine the impact of these changes on infants' mortality rates in twins and singletons . They found that multiple births experienced greater declines in infants mortality rates than singletons [4].

A study was done in University of Maiduguri Teaching Hospital and they found that the incidence of twinning was 14.4/1000 birth, and perinatal mortality rate was 85.4/1000 birth, which was significantly higher than that of singletons ($p<0.05$) [23].

1.3.2 Prematurity and intrauterine growth retardation :

The most important complication of pregnancy, is delivery before term especially before 32 weeks gestation. Almost all babies delivered before 24 weeks gestation die, and those above 32 weeks survive. Delivery between 24 and 32 weeks is associated with greater chance of neonatal death, and survivor suffers handicap [1].

The incidence of delivery between 24 to 32 weeks gestation is 1% in singletons, but it is 5% in dichorionic twins

and 10% in monochorionic twins .The average gestational age at delivery is 37 weeks, therefore, half the twins are delivered preterm [1].

Delivery of live-born neonate before 37th weeks gestation from the 1st day of the last menstrual period are termed premature by World Health Organization " WHO" .

Infants of extreme low-birth weight "ELBW" are less than one kilogram. Low-birth weight "LBW" infants are considered to be premature with shortened gestation age to have intrauterine growth retardation "IUGR" for gestational age referred to small for gestational age "SGA" or both .

Incidence of prematurity has been increased since 1981 due to the increase in preterm labour .

Very low-birth are predominantly premature (1.4%) and they are account for 50% of neonatal deaths and 50% of handicapped children.

Survival is directly related to birth weight with approximately 20%of those between 1250 and 1500 grams survived the first year.

Again the risk of rehospitalization is higher in preterm

compared to term babies [5].

A high prevalence of LBW infants due to prematurity and IUGR occurs more frequently in multiple pregnancy than in singleton pregnancy [2].

Again in an English study, birth weights for triplets and twins was evaluated .They found that triplets had a significant lower median birth weights and gestational ages [39].

Study was done in USA to compare mortality and morbidity of triplets to singletons and twins neonates during a 5 year period. The outcome was 55 triplets were compared to 959 singletons and 357 twins. The median gestational age of triplets at delivery was lower compared to those of twins and singletons [40].

In the University of Maiduguri Teaching Hospital study was done, again the frequency of preterm labour in twins was significantly higher than that of singletons [23].

In a study done in Ghana involving 623 twins, 1248 singleton births. Singletons were heavier than twins. The incidence of LBW, stillbirths and admissions to, and the stay in NICU were significantly higher in twins than singletons[7] .

In multiparous women ultrasound abdomen is the primary tool for monitoring fetal growth, a common policy of 4-weekly scanning from 24th week gestation. Monochorionic twins should be scanned at fortnightly intervals from 18th week gestation to allow early diagnosis and thus treatment of fetofetal transfusion syndrome and also because of greater risk of fetal compromise in one twin to its co-twin [41-43].

1.3.3 Hyaline Membrane Disease (HMD) :

HMD or Respiratory Distress Syndrome (RDS) incidence is inversely proportional to the gestational age and birth weight , so it primarily occurs in premature infant. It occurs in 60-80% of infants less than 28 week of gestational age, 15-30% of those between 32 and 36 week gestation , about 5% beyond 37 week gestation ,and rarely at term .An increased incidence is associated with multifetal pregnancies and asphyxia [5].

1.3.3.1 Aetiology :

Surfactant deficiency is the primary cause of HMD . Absence of pulmonary surfactant makes the lung liable to

atelactasis owing to increase surface tension. With progressive gestational age, increasing amount of surfactant is synthesized and stored in type II pneumocytes .

Surfactant is present in high concentration in fetal lungs by 20 week gestation but doesn't reach the surface of the lungs until later .

It appears in amniotic fluid between 28 and 32 week gestation .Mature level of pulmonary surfactant is usually present after 35 weeks.

1.3.3.2 Clinical features:

Signs of HMD usually appear within minutes after birth, although they may not be recognized for several hours in larger preterm infants until rabid shallow respiration has increased to 60/min. or greater. The late onset should suggest other diagnosis.

Characteristically: tachypnea, prominent grunting, intercostal and subcostal retractions, nasal flaring and duskiness are noted . In most cases the symptoms and signs may reach the peak within the third day, after which improvement is gradual. Death is rare on the first day of

illness and usually occurs between day 2 and 7, and associated with alveolar air leak (interstitial emphysema, pneumothorax) and pulmonary or intraventricular haemorrhage.

Mortality may be delayed weeks or months if chronic lung disease develops in mechanically ventilated infant [5].

1.3.3.3 Diagnosis:

Clinical course, chest x-ray, blood gases and acid base values help to establish the diagnosis. In CXR the lungs have a characteristic but not pathognomonic appearance which include a fine reticular granularity of the parenchyma and air bronchograms that are often more prominent early in the left lower lobe because of superimposition of the cardiac shadows. The initial CXR is normal sometimes and may need 6-12 hours to develop. The differential diagnosis includes sepsis , pneumonia (that present at birth in which CXR findings are like those of HMD), cyanotic heart disease, persistent pulmonary hypertension , pneumothorax, pleural effusion, diaphragmatic hernia and congenital anomalies, such as cystic adenomatoid malformation, pulmonary

lymphangiectasia or lobar emphysema[5] .

1.3.3.4 Prevention:

The most important is the prevention of prematurity. Administration of dexamethazone or betamethatzone to women 48hours before delivery of fetuses between 24 and 34 weeks gestation .These steroids also decrease the incidence of other complications of prematurity, such as IVH, pneumothorax, patent ductus arteriosus, and necrotising enterocolitis[5].

1.3.3.5 Treatment :

The basic defect requiring treatment is inadequate pulmonary exchange of oxygen and carbon dioxide. Early support of low-birth weight especially in the treatment of acidosis, hypoxia, hypotension and hypothermia [5].

Twins born at fewer than 35 weeks' gestation are twice as likely to develop RDS as single birth infants born at fewer than 35 weeks gestation, and the prevalence of RDS is greater in MZ than DZ twins. Concordance rate for RDS (i.e. both twins have RDS) is greater in MZ than in DZ twins. If the twins are discordant for RDS, then the second twin is more likely to

develop RDS than the first twin[44].

The well-known increased risk of RDS in the second twin as compared to the first twin is usually attributed to the second twin's predisposition to depression at birth (asphyxia). The etiological role of birth order was analyzed, presentation and asphyxia at birth in the development of RDS in matched case –control population drawn from 221 preterm twin pairs. Among the 39 twin pairs discordant for RDS, the second twin was affected member in 31 pairs. Second twins delivered abdominally did not have an increased risk relative to the first twins (odd ratio, zero to 17.8). When depression at birth was evaluated as an outcome of variable, malpresentation, rather than birth order was the major risk factor (independent matched odd ratio of 2.7 {confidence interval 1 to 7.5} and 1.3 {confidence interval 7 to 2.5 }, respectively). Thus, the 2nd twins' increased risk of RDS can not be explained by asphyxia at birth; a more important factor may be that the 2nd twins do not benefit from the salutary effect of labour to the same extent as the 1st [45] .

In Bulgaria, a retrospective study was done on all live

born children that died in the neonatal period for 5 years period of time. They are divided into two groups; twins and singletons. It established that neonatal mortality rate as a whole is decreasing while that of early neonatal mortality rate of twins is 3.6-4.5 times higher than that of singletons. Inside the twins who died in the neonatal period, 63.64% were with birth weight ≤1500g, while in singletons this percentage is 37.07%. The main reasons for death of twins are respiratory distress syndrome, intracranial haemorrhage and intrapartum asphyxia, followed by congenital malformations and infections[46].

In USA another study was done to compare the second twin outcome with that of the first twin. Twin pregnancies from 1989 through 1992 were reviewed retrospectively. Charts demonstrating both twins stillborns, either twin weighing < 500gm, or twins with a serious congenital malformation were excluded. After these exclusions, 200 twin pairs remained for analysis. Each twin is compared directly with its birth mate. The 1st twin is postulated as having the best possible outcome for the pregnancy involved, and the second-twin outcomes are

compared with these. The result is that the 2nd twins were more likely to be intubated, have RDS, need resuscitation, and have low 5-min Apgar score. Second twins have more nursery complications. The <1500gm group appeared to be at special risk, with more 2nd twin neonatal deaths and much higher rates of intubation and resuscitation(47)

1.3.4 Hypoxic-ischemia:

Asphyxia is the simultaneous occurrence of hypoxia and ischemia. The infant is born with depressed Apgar score, and failure to achieve a score of 5 by 5 minutes indicates significant asphyxia(48).

Apgar score is a practical method for immediate assessment of the neoborn after birth . It doesn't reflect the neonatal mortality or subsequent cerebral palsy . At one minute it is important to determine the need for resuscitation and other scores to detect the benefit of resuscitation (49) .

Hypoxic –ischemic encephalopathy is an important cause of permanent damage to the central nervous system cells, which may result in neonatal death or manifest later as

cerebral palsy or mental deficiency.

Fifteen per cent to 20% of infants with hypoxic-ischemic encephalopathy die in the neonatal period; 25-30% of survivors develop permanent neurodevelopmental abnormalities,

Asphyxia is considered in the presence of fetal acidosis "pH < 7.0", a 5-min Apgar score of 0-3, hypoxic-ischemic encephalopathy (altered tone, depressed level of consciousness, seizures), and other multiple organ system signs [5].

1.3.4.1 Aetiology:

- Fetal hypoxia may result from :
- Inadequate oxygenation of maternal blood as result of cyanotic heart disease, hypoventilation during anesthesia ……etc).
- Low maternal blood pressure as a result of hypotension that may complicate spinal anesthesia or may result from compression of inferior vena cava by gravid uterus.
- Inadequate relaxation of the uterus to permit placental filling as a result of uterine tetany caused by excessive

administration of oxytocin.

- Premature placental separation .
- Impedance to the circulation through the umbilical cord as result of compression or knotting of the cord .
- Newborns from multiple pregnancies have an increased risk of birth asphyxia from umbilical cord entanglement, locked twins, a prolapsed umbilical cord, uterine rupture and placenta previa.
- All the above mentioned aetiological factors use to occur in multiple pregnancies more than singleton pregnancies[5].

After birth hypoxia may result from:

- Anaemia severe enough to lower oxygen content of the blood.
- Shock (massive blood loss, intracranial haemorrhage…etc)
- A deficit in arterial oxygen staturation resulting from failure to breathe adequately postnatally owing to cerebral defect, narcosis, or injuries.
- Failure of oxygenation of an adequate amount of blood

resulting from severe form of cyanotic heart disease or lung disease[5].

1.3.4.2 Clinical features:

Signs of hypoxia in fetus are noted a few minutes to a few days before delivery. Intrauterine growth retardation with increased vascular resistance may be the first indication of hypoxia. The fetal heart rate slows, and the beat –to –beat variation declines. Fetal scalp blood analysis may show a pH less than 7.20, and continuous heart monitoring may reveal variable or late deceleration pattern. To avoid fetal death, particularly for those near term administration of high concentration of oxygen to the mother and immediate delivery are important issues. At delivery, the presence of meconium-stained amniotic fluid is an evidence of fetal distress. At birth these infants are depressed and fail to breathe spontaneously. During the coming hours, they may remain hypotonic, or may change from hypotonia to extreme hypertonia or their tone may appear normal. Pallor, cyanosis, apnea, slow heart rate and unresponsiveness to stimulation are signs of hypoxic-ischemic encephalopathy. Cerebral edema may occur in the

next 24 hours and results in profound brain stem depression. During this time seizures occur[5].

1.3.4.3 Treatment:

Therapy is supportive and directed at the organ system manifestation[5].

The second born twin is at greater risk of developing asphyxia than the first born. [45]

Some epidemiological characteristics of twin pregnancies and twin infants have been reviewed. The resulted twins are born prematurely and have lower birth weights than their singleton counterparts after 30 to 34 weeks gestation. Twins are also more prone to birth asphyxia, RDS, respiratory disorders, and seizures[50] .

In Nigeria an analysis of twins pregnancies to determine incidence of perinatal outcome of multiple pregnancies revealed that the perinatal mortality rate was 278.2\1000. The clinical cause of death was asphyxia in 2.4%of them[6].

Another study revealed that the risk of neonatal death , especially for term infants with asphyxia – related deaths , is

increased for the second twins who were delivered by C/S after vaginal delivery of the first twins. [51]

A study was done to examine trends in cause- and birth weight-specific fetal and neonatal mortality rates in twins and singletons. It was a descriptive analysis based on a regional register. A sample of 236 fetal and 356 neonatal twin deaths; 2,687 fetal and 2,301 neonatal singleton deaths from a population of 10,734 twins and 505,477 singletons. It was found that the extended perinatal mortality (including stillbirths and neonatal deaths) rate (EPMR) was 55.2 per 1,000 in 1982-1994 in twins compared with 9.9 per 1,000 in singletons. The relative risk for twin compared with singleton deaths was 5.6 (95% CI 5.1-6. 1) being highest for immaturity (12.9, 95% CI 11.1-15.0). A significant decrease in the EPMR occurred in both twins and singletons in 1988-1994 compared with 1982-1987. The EPMR decreased mainly due to a reduction of deaths from antepartum asphyxia in twins and intrapartum asphyxia and trauma in singletons, as well as a reduction in congenital malformations in both groups. In both

twins and singletons, birth weight-specific mortality rates improved between 1982-1987 and 1988-1994. It was concluded that the higher relative risk for twin deaths remained stable due to a similar decrease in the EPMR for both twins and singletons. The cause-specific relative risk in twins declined for antepartum asphyxia. The mortality rate resulting from lethal congenital malformations decreased in twins and singletons mainly due to earlier detection and subsequent termination of pregnancy. [52]

Compared with the first twin , the second twin is at increased risk of RDS and asphyxia.[53]

Another study was done in Japan to evaluate the prevalence of cerebral palsy in twins, triplets and quadruplets. The subject was 705 twins pairs (1410 twins), 96 offset of triplets (287 triplets excluding one infant death), and 7 sets of quadruplets (27 quadruplets excluding one infant death), who were born after 1977.

The prevalence of C.P was 0.9% among 1410 twins, 3.1% among 287 triplets and 11.1% among 27 quadruplets.

Furthermore the risks of producing at least one child with CP were 1.5%, 8% and 42.9%, in twins, triplets and quadruples, respectively. After adjusting for each associated factor using logistic regression, the risk of C.P was significantly associated with decrease in gestational age and asphyxia. The odd ratio indicated that infants whose gestational ages of < 32 weeks were 20 times more likely to develop C.P than infants whose gestational ages were more or equals to 36 weeks. Thus concluded that the prevalence of C.P in triplets and quadruplets is higher than that of twins, and lower gestational age was associated with a greater risk of C.P[54].

1.3.5 Sudden Infants Death Syndrome "SIDS":

It is defined as sudden death of an infant that is unexpected by history and unexplained by a thorough postmortem examination that included autopsy, investigations of the scene of death, and review of the medical history .

An autopsy is essential in all unexplained infants death because the history and scene investigations do not preclude all known causes of sudden infant death (i.e. congenital heart

or brain abnormalities, and fatal child abuse).SIDS is the most common cause of infants mortality in United States after congenital malformations and disorders related to short gestation\low-birth weight.

About 3000 infants in USA in 1996 died of SIDS. A rate of 0.74\1000 live birth in full-term infants of SIDS is rare before one month of age[55].

A few previously unrecognized congenital malformations of the heart are discovered at autopsy. Most newborn babies are obligatory nasal breathers. It is possible that sudden nasal obstruction from an upper respiratory tract malformations could be the cause of death. SIDS occurs more frequently in infant born from multiple pregnancy than in singleton infant, and the incidence is particularly high among twins weighing < 2 kg at birth [56-59]

The risk of SIDS is increased by a prone or side sleeping position and loose bedding which can slip over the baby's head. A sleeping position on the back is recommended [60-62].

Exposure of babies to tobacco smoke from other members of the household before or after birth increases the risk of death: the greater the exposure the higher the risk [63, 64]. 62.6% of mothers with babies who died from sudden infant death smoked as compared to 25.1% of mothers in the case-matched control group [63].

Health promotion campaigns directed towards the reduction of sudden infant death syndrome should be aimed specifically at more socially deprived families who do not share in the general fall in the incidence of this condition [65].

1.3.5.1 Pathology:

The autopsy findings are only suggestive but not conclusive. For example, you may find pulmonary odema and diffuse intrathoracic petechiae. Also demonstration of structural evidence (tissue markers) of chronic asphyxia in two-third of them.

Brain stem abnormalities in SIDS victims include: local astrogliosis, persistent dendrites spines, and hypomyelination.

Significant increase in the number of reactive astrocytes in the medulla also have been observed. Substance P, a neurotransmitter peptide found in selected sensory neurons of the central nervous system, is present in increased amount in SIDS victims. The most compelling hypothesis to explain SIDS is a brain stem abnormality in cardiorespiratory control, including arousal responsiveness, and perhaps other controls such as blood pressure. Among epidemiological factors there are maternal and antenatal factor like intrauterine growth retardation, anaemia, intrauterine hypoxia and increased parity, conditions that strongly associated with multiple pregnancies [55].

Adeson and kinney conducted a comprehensive survey of infant death involving 126 cases. The study found that 3 infants of the 126, who died, had twin siblings. In all 3 cases in this study, the twin siblings survived [66].

Coe and Hartman conducted another study of 84 infants dying during 18 month period . 3 of the 84 who died had twin siblings who survived[67].

Kraus and Borhani studied 719 infants who died in

California in 1968 and documented that one set of twin died on the same date [68].

Valdes-Dapena in reviewing the progress in understanding sudden unexplained infant death between 1970- 1975 also described one set of twins who died on the same date . Valdes-Dapena noted that both infants has increased level of oxalic acid at time of death, but no explanation of it's significance was present. Valdes – Dapena commended that the increase of sudden death for the infant born of multiple birth, is likely to be due to decreased birth weight [69].

Spiers analyzed data collected for 8967 twin pairs born in North California between 1955 – 1967. He calculated concordancy rates and dependency ratio for members of like – sex twin birth who died at 7 to 364 days of age. In this population there were 17sets of twins of both members died at home; in 14 instances, the co-twins died within 30 days after the death of the first twin. In 9 instances, the twin died in the same day. Spiers speculated that simultaneous death from SIDS could be due to transient common experience occurring

shortly before death, basing on the fact that the excessive risk of death for the survived twin is limited to a period of one month [70].

A study done in South Australia, from 1970 to 1988. 33 twins infants were found unexpectedly dead while the co-twin was alive. Of these infants, 31 died of SIDS. The incidence of SIDS for twins who were significantly growth retarded compared with the co-twin, was 6 in 135, a rate of 44 per 1000. Follow-up had been possible for 22 twins. Of these 22 twins, asthma developed in 9 and recurrent pulmonary infections in another 2 children. One pair of twins were found dead at the same time. The other 32 co-twins remain alive. According to literature review, unless both twins died within 24 hours, SIDS in surviving co-twins of an infant died of SIDS is rare (1%) [71].

Another study in Germany, where 429 SIDS cases were investigated in a retrospective study. In this study, the death in which at least one brother or sister had died under comparable circumstances was evaluated. The 429 who died comprised 17 multiple-birth babies (3.7%) including 15 twins

and 2 triplets. Eleven cases (2.6%) were brothers or sisters of SIDS victims.

Three cases who were the relatives of the babies' mother had died of SIDS. A comparison of various cases groups did not reveal any patho-morphologically significant difference between the groups or difference from other SIDS cases. All the multiple-birth babies were premature babies. There was a raised incidence of poor socio-economic condition in the sibling group.

The results are significant for parents counseling, preventive measures and the detection of concurrent (in particular, unnatural) cause of death [72] .

Between 1993 and 1998 data from the Office National Statistics on all registered live births and infant death with registered cause of death in England and Wales were obtained, together with the registered birth weight and for twins, whether they were like or unlike sex. They found that the risk of SIDS in twins is twice that of singletons, this is mainly attributed to the higher proportion of twins being of LBW [73].

1.3.6 Congenital Malformations:

Any anatomical defect present at birth is classified as congenital malformations. This term has no aetiological implication and must not be misused as a synonym for hereditary disorders[74].

1.3.6.1 Fetal abnormalities:

The prevalence of structural abnormalities, such as spina bifida, for each fetus in a dichorionic twin pregnancy is the same as in singleton pregnancies, and therefore the chance that in such twin pregnancies at least one high as in singleton pregnancies.

In monochorionic twin pregnancies the risk of abnormalities for each fetus is four times as higher as in singleton pregnancies. Multiple- gestations showing abnormality in one fetus can essentially be managed expectantly or by selective feticide of the abnormal twin. In cases where abnormality is a non-lethal but may well result in handicap, the parents need to decide where the potential burden of a handicapped child is enough to risk the loss of the normal twin from fetocide related complications. In cases

where the abnormality is lethal it may be best to avoid such risk to the normal fetus, unless the condition itself threatens the survival of the normal twin.

Anencephaly is a good example of a lethal abnormality that can threatened the survival of the normal twin, because in more than 50 percent of pregnancies affected by fetal anencephaly, there is a polyhydramnios which can cause preterm delivery of both normal and abnormal twins [1].

1.3.6.2 Chromosomal defects and twining :

In monozygotic twin pregnancies, chromosomal abnormalities such as Down's syndrome, affect either none or both fetuses. The risk for chromosomal abnormalities, as in singleton pregnancies, increases with maternal age.

In dizygotic twins, the maternal age related risk for chromosomal abnormalities for each twin might also be the same as in singleton pregnancies. Therefore the chance that at least one fetus is affected by a chromosomal defect is twice as high as in singleton pregnancies of the same maternal age. However, the rate of dizygotic twining increased with maternal age, and in addition , with the more wide spread availability of

assisted reproductive techniques, the mean maternal age in dizygotic twins is increasing . Consequently, the overall prevalence of the chromosomal defect in dizygotic twins is higher than in singletons.

The relative proportion of spontaneous dizygotic to monozygotic twins in United Kingdom is about 2:1 and therefore, the prevalence of chromosomal abnormalities affecting at least one fetus in twin pregnancies overall would be about1.6 times that in singletons.

If the pregnancy is dichorionic, the parents can be counseled that the risk of one fetus developing a chromosomal abnormalities is about twice that in singleton pregnancy. The risk that both fetuses would be affected can be derived by squaring the singleton risk ratio, for example in a 40 years old woman with risk of trisomy 21, based on maternal age, of about 1 in 100, in dizygotic twin pregnancy, the risk that one fetus would be affected is 1 in 50 (1 in 100 plus 1 in 100).

However, the risk that both would be affected is 1 in 10.000 (1 in 100 X 1 in 100)[1].

1.3.6.3 Larngotracheoesophageal Cleft (LTOC) and Unilateral Pulmonary Hypoplasia (UPH) in twins:

Larngotracheoesophageal cleft (LTOC) and unilateral pulmonary hypoplasia (UPH) are rare congenital anomalies which have not been considered related [75,76]

The most commonly associated anomaly has been oesophageal atresia/ tracheoesophageal fistula and the extend of the cleft has not been correlated well with the presence of other anomalies [74] .

Tracheobronchial malformations were reported only in three instance, tracheal stenosis in two and hypoplastic cleft bronchus and lung in one [74-77] .

Unilateral pulmonary hypoplasia / atresia has been associated with esophageal atresia / tracheoesophageal fistula in 5% to 10 % of cases but coincident LTOC has not been reported [78,79] . Both syndromes have been associated with bony and lower gastrointestinal abnormalities. The mirrorimge hypoplasia in these twins leads to speculation about basic mechanism of pathogenesis. Pulmonary hypoplasia / a plasia have been reported in several twin pairs, concordant atresia,

mirrorimage atresia and atresia involving only one twin have been observed [80].

- *Other causes:*

Twin to twin transfusion and congenital anomalies occur predominantly in monozygotic twins. Anomalies are due to crowding, vascular communication with embolization, and with unknown factors that cause conjoined twin. [81]

1.3.7 Fetal Transfusion Syndrome :

Placental vascular anastomoses occur with high frequency only in monochorionic twin. In monochorionic placentas the fetal vasculature is usually joined, sometimes in a very complex manner. The anastomosis may be artery to artery, vein to vein, or artery to vein. In this abnormal phenomenon, the hemodynamic is well balanced by smaller deep unidirectional arteriovenous anastmoses, so that neither twin suffers. Artery-to- artery communication cross over placental veins, and when anastomoses are present, blood can readily be stroked from one fetal vascular bed to the other.

Vein-to- vein communications are less common. A

combination of artery -to- artery and vein-to- vein anastomoses is associated with the lethal a cardiac fetus. This rare anomaly (1:35000) is secondary to twin reversal arterial perfusion (TRAP sequence).

The a cardius results from chronic shunting of reserved deoxygenated arterial blood which is associated with only rudimentary development of the upper body structures including the heart [32].

In rare cases one umbilical cord may arise from the other after leaving the placenta, here the twin attached to secondary cord is usually malformed or dies in utero [5].

Feto-fetal transfusion syndrome “FFTS” occurs in 4-20% of monochorionic twins and has 15% perinatal death. It involves chronic shunting of blood. The donor arterial side is small with anhydramnios (stuck twin), anaemic, small and premature, hypovolaemic with small or normal glumeruli. The recipient (venous side), is polyuric with polyhydramnios, large premature, plethoric polycythemic, hypervolamic with myocardiac dysfunction, tricuspid regurgitation and may suffer hydrops [32].

Generally with chronicity there is a 5 g/dl hemoglobin and 20% body weight difference in this syndrome. Transfusion when occurs and the recipient dies , in utero, there is 25% risk of ischemic, neurologic and renal lesions occur in survivor. Although previously was attributed to disseminated intravascular coagulation "DIC" or transfusion of thromboplastin, the mechanism is now known to be acute transfusion from healthy twins' circulation to dying hypotensive twins' circulation [32].

In UK thirteen fetuses (five twin, and one triplet) were compromised by feto-fetal transfusion syndrome in six pregnancies, five twins in the midtrimester, and one triplet in the third trimester. This diagnosis which was suspected because of ultrasound finding of discordant growth, discordant amniotic volumes, concordant external genitalia, and monochorial placentation, was confirmed postnatally in each. Nine fetuses underwent blood sampling to aid diagnosis and fetal well-being. In contrast to FFTS investigated postnatally, a difference of hemoglobin concentration of 50g/dl or more in utero was found only in one pregnancy,

which was near term, although all had fetal erythroblastaemia and a difference in weight of 20% or more in vivo confirmation and shared circulation is achieved in two pregnancies by transfusing adult rhesus negative red into the smaller fetus and then detecting them by Kleihauer testing in blood aspirated from the larger. Invasive procedure also yielded information in fetal blood gas measurement (acidosis in four and hypoxemia in six) and amniotic pressure (raised in two), they suggest that comparison of hemoglobin concentration is inaccurate in FFTS in utero, the diagnosis of which may necessitate detection of adult red cells [82].

Another report from Germany of feto-feto-fetal triplet transfusion syndrome “FFFTS” in spontaneous monochorionic trimesteric triplet pregnancy primarily diagnosed at 17 weeks of gestation. During the course of pregnancies, sequentially two triplets appeared as donors. Symptoms of recipient such as polyhydramnios … etc, were present in the third triplet, twin in utero at twenty-five weeks gestation. At twenty seven weeks gestation, a cesarean section was performed mainly due to pre-eclamsia. The first donor triplet developed normally,

whereas the recipient showed periventricular leucomalacia and neurological impairment [83].

In Germany a paper described the initial experience with Laser – Induced Interstitial Thermotherapy (LITT) for the treatment of TTTS. This procedure was utilized in four pregnancies at (twenty–twenty six weeks of gestation) with server TTTS with fetal dropsy, polyhydramnios of the acceptor, and anhydramnios of the donor. In vitro examination of the placental tissue had shown that laser coagulation can be monitored sonographically, hence we used this method for the first time in these four pregnancies. Blood vessels connecting the two umbilical cords were determined prior to the treatment using the new ultrasound color techniques which was highly sensitive and capable of representing slow blood velocity. A 1.2 mm thick puncture needle was then directed to the shunt under on-line ultrasound control. All patients had an anterior wall placenta. The laser fibres were inserted via this thin needle a coagulation of two to three minutes was necessary at 3w. in one twin pregnancy the intrauterine fetal death of the smaller child occurred ten weeks after LITT, the other child

survived and was healthy. A cesarean section was necessary in another twin pregnancy one week after LITT due to the intrauterine death of the smaller child. In the third twin pregnancy, the donor who had already had distinct bradycardia prior to the treatment, died immediately after LITT. The intrauterine fetal death of the donor in the triplet pregnancy occurred 3 days after LITT once the volume of the amniotic fluid had basically returned to normal. The tragic intrauterine death of the uninvolved child occurred 13 weeks later as a result of umbilical cord strangulation. The surviving child is healthy. All four pregnancies were severe and advanced cases of TTTS with a very poor prognosis, leaving us with no other alternative to the described methods of treatment. The instruments we used were a lot thinner than those utilized for fetoscopic laser treatment to date [84]. It is a rare occurrence in manozgotic twins. Triplet pregnancy composed of an acardiac fetus and a pair of conjoined twins is even more rare. The outcome of acardius is invariably fatal, and the mortality rate of other fetus ranges between fifty and seventy percent. Perinatal mortality results mainly from

complications of twin-to-twin transfusion syndrome. Case: intrauterine fetal death, caused by an umbilical cord accident, with twisting of the acardius's cord around the fused cord of the conjoined twins is reported and they concluded that an acardius should be thoroughly sought when monochorionic multiple pregnancy is found by ultrasound during prenatal care. The complications of pregnancies caused by an acardius fetus can be avoided by using proper management [85].

To improve the outecome of severe twin -to- twin transfusion syndrome with 1 hydropic fetus and to prevent ischemic sequelae in the survivor, a technique of selective feticide by vascular embolization of the most severely damaged twin was developed. Acute second trimester polyhydramnios occurred in 4 biamniotic monochorial twin pregnancies, with 1 fetus normal on ultrasound. The hydropic fetus underwent embolization using a bolus of histoacry1 injected into the umbilical vein and fetal heart under ultrasound guidance. In 1 triplet pregnancy with a set of monochorial fetuses, premature labor occurred at 26 weeks, 2 weeks after embolization, and there were 2 neonatal deaths. The 3 others resulted in the

birth of a normal infant at 31-37 weeks of gestation. This suggests that in twin -to- twin transfusion syndrome with severe polyhydramnios and hydrops of 1 fetus, embolization may salvage the other twin [86].

1.3.8 Twin Transfusion Causing Cutaneous Erythro poiesis:

In a report of two cases of twin-to-twin transfusion syndrome (TTTS) in which prolonged intrauterine anaemia in the donor twin was associated clinically with a blueberry muffin skin lesions and histologically with cutaneous erythropoiesis. These skin lesions are 2-to-8 mm, bluish-red macules and papules. In the newborn, these lesions are seen in a variety of non-inflammatory cellular infiltrating diseases, including the malignancies of congenital leukaemia, and neuroblastoma [87-89].

Cutaneous erythropoiesis of a non-malignant causes is most often associated with intrauterine viral infections, especially rubella [90]. In a single case reported in a literature,

intrauterine anaemia due to spherocytosis, has been associated with cutaneous erythropoiesis [91].

Perfusion of monochorial twin placenta shows twin-to-twin vascular anastomoses with considerable frequency [92] unbalanced placental circulation favouring one of the twins over the other leads to twin-to-twin transfusion, and more than 10% of monochorial twin pregnancies exhibit the TTTS, which account for greater fetal and neonatal risk in monochorial than in dichorial twin gestation [93].

The skin is also an organ of erythropoiesis during embryonic development, beginning at the 8-mm stage until the age of the 5th intrauterine month, when myelopoietic differentiation also begins in the dermis, and erythroplastic elements seem to be phagocytized by developing leukocyte [94].

At the other end of the age spectrum, recurrence of dermal hematopoiesis has been documented in several cases of myelofiborsis, whether this represents a response to a prolonged, severe anaemia from bone marrow failure, or malignant clone of cells is unclear [95].

♣ JUSTIFICATIONS

- Multiple-birth neonates have significant mortality and morbidity.
- Anticipation and early detection of complications related to multiple-birth newborns would prevent a lot of cases of death and future handicaps .
- Very few studies were done in Sudan .

♣ OBJECTIVES

- To determine intranatal and early neonatal mortality and morbidity of multiple-birth newborns in 3 hospitals in Khartoum state .

- To identify maternal risk factors associated with Multiple-birth newborns.

2- MATERIALS AND METHODS

2.1 Study Design:

Prospective descriptive case-control hospital – based study .

2.2 Study Area:

Omdurman Maternity Hospital (O.M.H) Khartoum Teaching Hospital (K.T.H) and Khartoum North Teaching Hospital (K.N.T.H)

2.3 Study period :

From the first of July to the first of December 2004.

2.4 Study Population:

Multiple-birth newborns and singletons from birth to day 7, together with their mothers who delivered at O.M.H , KTH and KNTH, in a three days a week .

The above hospitals represent the main hospitals in each city, being the major target for the population. For this reason they were selected.

2.5 Sample Size:

$n = z^2 pq/d^2$

n= Sample

z =Statistical certainty = 1.96

p = Prevalence =0.05

q =Probability of failure = 1-0.05 =0.95

d = Desired margin of error =0.05

n =73

A control group of 73 mothers and singleton newborns who were delivered at the same day , the same Hospital and to the nearest gestational age .

2.6 Inclusion Criteria :

Multiple-births newborn and singletons (including still birth) delivered at the same day, the same hospital, and to the nearest gestational age from birth to day 7, together with their mothers (either delivered abdominally or vaginally).

2.7 Exclusion Criteria:

2.7.1 Newborns of mothers with any disease that might adversely affect the fetuses, such as pregnancy induced hypertension, diabetes mellitus, rheumatic heart disease, anemia…etc.

2.7.2 Loss of contact with the newborn in or after day 7 .

2.8 Study Technique:

A written consent was take from :

2.8.1 Parents.

2.8.2 Hospital manager.

2.8.3 Department of Obs and gynae.

2.8.4 Neonatal care unit.

2.9 Research Tools:

2.9.1 A structured questionnaire consisting of 29 items which can be delineated into 4 parts:

2.9.1.a The 1st part consists of direct interview with the mother dealing with relevant history.

2.9.1.b The 2nd part deals with initial examination and resuscitation of the newborns .

2.9.1.c The 3rd part deals with detailed examination of the newborns .

2.9.1.d The 4th part deals with follow –up of the newborn and relevant investigations .

The questionnaire parts B, C and D were repeated for the 2nd and 3rd born infants for the control group, part A was repeated for the mothers, B and C were repeated for the newborns.

2.9.2 Measurements: The authors attended deliveries and immediately after birth he determined the length using anon-stretchable tape, the head circumference to the nearest 0.1cm; again using a non-stretchable tape, and the weight using Salter scale, and the reading was taken to the nearest 10 grams.

2.9.3 The author determined the gestational age using Expanded New Ballards Score (NBS) [5].

- Maternal interview : The author Interviewed(case and control), collected the data concerning the age , parity

ethnic group family history and past history of multiple pregnancy together with the use of ovarian stimulants and the mode of delivery.

- Initial examination of the newborns: The author attended deliveries and examined the newborns immediately after birth and determined their APGAR score and subjected them to resuscitation when appropriate .
- Detailed examination of the new born: Also the newborns where examined in details (routine neonatal examination) for evidence of organ system problem, gestational age assessment and congenital malformations.

Follow-up of the newborn:

The in-patients were followed-up during their stay in hospitals and investigated when relevant. The out-patients were telephoned or visited at home on or after day 7.

2.10 Research Team:

The researcher and two paediatrics registrars attended the deliveries .Obstetric registrars on call was used to telephone the author when there was multiple birth deliveries .

2.11 Statistics Analysis :

The data were analyzed by computer using SPSS (statistical package for social science) , the $x^{2.}$ test was used for the difference in proportion . P. value of <0.05 was regarded as statistically significant .

2.12 Difficulties confronted the study:

2.12.1 Refusal of some parents.

2.12.2 Occurrence of more than one delivery at more than one hospital at the same time in one occasion .

2.12.3 Follow-up of the patient.

3- RESULTS

During a period of 5 months , 222 babies were delivered [70 pairs were twins (140 babies), 3 sets were triplets (9 babies) and 73 singletons as a control]. They were delivered at 3 hospitals, namely, Omdurman Maternity Hospital, Khartoum Teaching Hospital and Khartoum North Teaching Hospital . At the same time, 146 mothers (73 of them as a control) were included in this survey, replied to the first part of the questionnaire.

The distribution of birth was 135 in Omdurman Teaching Hospital, 57 in Khartoum Teaching Hospital and 30 in Khartoum North Teaching Hospital (Table 1)

3.1. Birth Weight:

The distribution of birth weight of the first, second and third twins together with that of the control is shown in (Table 2).

Four (5.5%) of the 1st twins and 6 (8.2%) of the 2nd twins have weights between 0.5 and 0.99kg . Ten (13.6%) of the 1st twins , 8(11%) of the 2nd twins, have weights between 1 and 1.49kg . Thirteen (17.8%) of the 1st twins ,11(15%) of the 2nd twins , and 2(66.7%) of the 3rd twins have birth weights between 1.5 and 1.99kg. 27 (37%) of the 1st and 28 (38.4%) of the 2nd twins , have weight between 2 and 2.49kg . An equal number of the 16(21.9%) of both 1st and 2nd twins have birth weight between 2.5 and 2.99kg . Two(2.8%) of the 1st twins and 4(5.5%) of the 2nd twins , have birth weight between 3 and 3.49kg .One(1.4%) of the 1st twins has birth weight between 3.5 and 3.99kg .

On the other hand, the singletons birth weights were as follow : 1(1.4%) has weights between 1-1.49kg, 2(2.8%) have weights between 1.5-1.99kg, 4(5.5%) have weights between 2-2.49kg ,23(31.5%) have weights between 2.5-2.99kg, 39(53.2%) have weights between 3-3.49kg , 2(2.8%) have weights between 3.5-3.99kg and 2(2.8%) have weights between 4-4.49kg (i.e. large for gestational age) .

The P. values for the 1st, 2nd and 3rd twins were 0 .00001,

0.0001 and 0.00002 respectively, which is statistically significant.

3.2 Centile of Birth Weight:

Table (3) shows that 1(1.4%) of the 1st twins and 2(2.8%) of the 2nd twins were below the 3rd centile i.e. (severe small for gestational age).

Thirty-one (42.4%) of the 1st twins, 29(39.7%) of the 2nd twins lie between the 3rd just below the 10th centiles.

Thirteen (17.8%) of the 1st twins, 7(9.6%) of the 2nd twins lie between 10th and just below 25th centiles .

Twenty- eight (38.4%) of the 1st twins , 35(47.9%) of the 2nd twins lie between 25th and just below 50th centiles. Concerning the 3rd twins , 1(33.3%) lies below 3rd and equal numbers lie between both the 3rd and just below the 10th centile.

Again there is a significant difference between these multiple- births newborns centiles compared to those of control ,since 6 (8.2%)of the control lie between 3rd and just below 10th centile ,7 (9.6%) of them lie between 10th and just

below 25th centile , 12 (16.4%) of them lie between 25th and just below the 50th centile , 44 (59.8%) of them between 50th and just below 75th centile ,2 (2.8%) between 75th and just below 90th centile and 2 (2.8%) of them were above the 90th centile (i.e. large for gestational age) .

The P. value was 0.000 for 1st and 2nd twins which is significant , and 0.3 for the 3rd twins which is not significant.

3.3 Birth weight to gestational age:

The relationship between birth weight and gestational age had been drawn on (Figure 1). 51.5% of the 1st born infants were appropriate for gestational age, while 45.5% were SGA. Concerning the 2nd born infants, 57.5% were AGA and 42.5% were SGA. About the 3rd born infants, 66.7% were SGA and 33.3% were AGA. In the control group (singletons), 89% were AGA, 8.2% were SGA and only 1 (2.8%) was LGA. The p value were 0.0003, 0.000 and 0.32, respectively.

3.3. Gestational Age:

These are shown in Fig. (2). 1st and 2nd twins have the same gestational age distributions, with 13 (17.8) of each have gestational age between 28 and 32 week. Fifteen (20.5%) of each lie between 33 and 36 weeks, 45 (61.7%) of each lie between 37 and 42 weeks. One (33.3%) of the 3rd twins has gestational age between 28 and 32 weeks , and 2 (66.7%) of the 3rd twins lie between 33 and 36 weeks gestation .

In the control group, only 1 (1.4%) is delivered between 28 and 32 weeks gestation, 2 (2.8%) between 33 and 36 weeks, and the remaining 70 (95.8%) were delivered between 37 and 42 weeks gestation.

P. value for 1st , 2nd and 3rd twins were 0.0002, 0.0002 and 0.0004 respectively i.e. there is a significant difference in birth weight in relation to gestational age in different groups compared the control.

3.5. Sex :

Figure (3) illustrates the sex distribution. Of the 1st 2nd, 3rd twins and control, 41(56.2%), 39 (53.4%) , 1 (33.3%) and 43(58.9%) respectively , were males.

The total number of the males is 124 out of 222, representing male/female ratio of 0.56. Of the 70 twins pairs and 3 sets of triplets ,17 pairs were of the same sex .

3.6. Apgar Score:

Table (4) showed that 2 (2.8%) of the 1st born infants, 4 (5.5%) of the 2nd born infants and 1 (33.3%) of the 3rd born infants, were asphyxiated (1 minute Apgar score of $\leq$ 3). P values were 0.0005, 0.000 and 0.000, respectively.

While (Table 5) showed that 2 (2.8%) of the 2nd born

infant and 1 (1.4%) of the control had a 5 minutes Apgar score of < 5, i.e. asphyxiated. P value = 0.06.

Table (6) showed the relationship between asphyxia and gestational age, in the 1st vs, 2nd born infants. Of those who had been delivered between 28 and 32 weeks gestations, only

1 infant of the 1st born ones had developed asphyxia compared to 4 infants who were born 2nd. Between 33 and 36 week gestation, the 1st and 2nd born infants were equally affected (one each). Between 37 and 42 weeks gestation only 1 infant is affected by asphyxia and this is the 2nd born one.

3.7. Respiratory Distress Syndrome:

The relationship between gestational age of various group including the control, and the development of RDS has been drawn on Figure (4). Six (8.2%) of the 1st twins who were delivered between 28 and 32 weeks gestation ,compared to 12 (16.4%) and 1(1.4%) in 2nd and singletons respectively . Of those who were delivered between 33and 36 weeks , only 1 (1.4%) of the 1st twins and a similar number in the 2nd twins developed RDS. The relationship between RDS and gestational

age was not significant between 1st , 2nd ,3rd and control (P = 0.84) .

3.8. Neonatal Sepsis:

Table (7) compares the relationship between gestational age and neonatal sepsis . Of those who were delivered between 28 and 32 weeks gestation, 2 (2.8%) of the 1st twins, 3(4.1%) of the 2nd twins and 2(2.8%) of the control contracted neonatal sepsis, while 2(2.8%) of the 1st twins, 4(5.5%) of the 2nd twins and 1(1.4%) of the control , whom they were delivered between 33 and 36weeks gestation ,had contracted neonatal sepsis.

In these findings neonatal sepsis is not related to multiple birth newborns P= 0.74 and 0.51 for the 1st and 2nd twins respectively .

3.9. Physiologic Jaundice:

Physiologic jaundice was not found to be affected by twining. Table (8) , which shows that 1 (1.4%) of the 1st twins ,

2(2.8%) of the 2nd twins and 1(1.4%) of the control who develop mild to moderate jaundice on the 3rd day of life , have birth weights between 1and 1.49kg . Two (2.8%) of the 1st twins ,3 (4.1%) of the 2nd twins and 2(2.8%) of singletons have birth weights between 1.5and 1.99kg .Only 1 (1.4%) of the 1st twins

has birth weight between 2 and 2.49kg . The 3rd twins were not affected . There is no relationship between birth weight and development of jaundice in different groups (P. values were 0.64 and 0.57 for 1st and 2nd respectively).

3.10. Congenital Malformations :

Of all deliveries (multiples and singletons) , only 1 (1.4%) of 2nd twins was affected (Omphalocele). This was referred to paediatrics surgery and operated on by the 4th day of age and readmitted again and died on the 7th day as shown in (Figure 5)

3.11 Relationship between birth weight and mortality in multiple-birth and singleton newborns.

Concerning the 1st born infants, 5 (6.8%) who weighted

0.5 – 0.99 kg had died and only 1 (1.4%) whose weight was between 1 – 1.49 kg had died. About singletons, only 1 (1.4%) whose weight was between 0.5 – 0.99 kg had died. P value = 0.08. Also there is statistical difference between the 2nd born infants and control, since 11 (15%) of the 2nd twins who

had died had birth weight between 0.5 – 0.99 kg, 1 (1.4%) had birth weight between 1 – 1.49 kg and 1 (1.4%) had birth weight between 1.5 – 1.99 kg. P value = 0.039

Only 1 (33.3%) of the 3rd born infants whose weight was between 0.5 – 0.99 kg had died compared to only 1 of the control group. P value = 0.15. (Table 9)

3.12. The Outcome By The End of the 1st Week:

Table (10): The ultimate outcome by the end of 1st week: disclosed that 10 (13.7%) ,6 (8.2%),and 1(1.4%) of the 1st twins, 2nd twins and control , respectively were still in NICU. This is statically significant i.e multiple births is strongly linked to admission to NICU (p= 0.0009).

Also it disclosed that 6 (8.2%) , 13 (17.8%) , 1 (33.3%) and 1 (1.4%) of the 1st , 2nd , 3rd twins and control , respectively where died (four of the multiple-birth newborns

where stillborns). Multiple birth is highly associated with early neonatal death compared to singletons (p=0.0003) .

The overall mortality rate of multiple births was 134.2 /1000 . That of the 1st twins was 82.1 /1000 , of the 2nd twins was 178/1000 , of the 3rd twins was 333.3 /1000 , and of the

control 13.7/1000. The sum total mortality rate was 94.6/1000 .

3.13. Ethnic Group:

The distribution of racial group in relation to whether the pregnancy is multiple or not is found in Table (11) . Twenty-nine (39.7%) of the respondents (case) were northern , 1(1.4%) were eastern , 15 (20.5%) were western, 8 (11%) were southern and 20 (27.4%) were central. The control group comprises 37 (50.7%), 1 (1.4%), 14 (19.2%), 4 (5.5%), 17 (23.3%) as northern, eastern, western, southern and central, respectively.

There is no relationship between ethnic group and multiple gestation (P. = 0.63) .

3.14. Parity:

There is strong relationship between multiple pregnancy and parity (the higher the number of parities , the

greater is the chance for multiple gestation) .(P. value 0.001)

Table (12) highlightened that 17(23.3%) of the mothers (case) were primigravidae , 10 (13.7%)had given birth to 2 children , 9 (12.3%) had given birth to 3 children , 12 (16.4%)

had given birth to 4 children, 12 (16.4%) had given birth to 5 children and 13 (17.9%) had delivered 6 children . The respective numbers of control were 36 (49.3%),13 (17.9%), 12(16.4%) ,4 (5.5%) , 6 (8.2%) ,2 (2.8%) .

3.15. Family history :

There is strong association between the family history and multiple pregnancy, Figure (6). Sixty one (83.6%) of the women (case) have family history of multiple pregnancies , compared to 33(45.2%) of those who have single pregnancies . (P. value =0.00001)

3.16. Past History:

Of the respondents (case) , 2(2.8%) had a past history of multiple pregnancies, compared to1(1.4%) of the control group as shown in Figure (7). The past history is not

associated with multiple pregnancy (P = 0.055).

3.17. Method of Conception:

In Figure (8) only 1 (1.4%) woman has had ovarian stimulant, and this was in the control group. There is no

relationship between multiple pregnancy and the use of ovarian stimulants. (P = 0.317)

3.18. Mode of Delivery:

The link between multiple pregnancy and abdominal delivery (cesarean section) is highly significant. Figure (9) shows that 9 (12.3%) of the women (case) had delivered abdominally ,while only 2 (2.8%) of the control had delivered abdominally (P value = 0.028).

3.19. Maternal Age :

Table (13) assesses maternal age. 2 (2.8%) of the mothers (case) and 12(16.4%) of control were between 15 and 19 years of age. 19 (26%) of the mothers (case) and 28 (38.3%) of the control were between 20 and 24 years . 16 (21.9%) of the mothers (case) and 20 (27.3%) of the control were between

25 and 29 years . 22 (30.2%) of the mothers (case) and 9 (12.3%) of the control were between 30 and 34 years . 12 (16.4%) of the mothers (case) and 3 (4.1%) of the control were between 35 and 39 years .

One (1.4%) of the mother (case) and 1(1.4%) of the control were between 40 and 44 years. One (1.4%) of the control group was above 45 years. The relationship between maternal age and multiple pregnancy is highly significant. (P = 0.002).

4- DISCUSSION

The study was done to determine intranatal outcome of multiple-birth newborns and maternal risk factors associated with multiple pregnancies.

The sex distribution showed that there is slight increase in males number (124 out of 222 were males). The number of male in singletons alone was 43(about 20% of all deliveries) . 17 pairs of multiple birth neoborns were of like- sex . Fig. 3 .

Although this study was limited by its small numbers , the finding of the two groups being compared support the contention that a large proportion of these data were statistically valid .

Multiple pregnancy affects the birth weights of newborn infants, that is to say it leads to intrauterine growth retardation.

In this study about two-fifths of multiple-birth newborns were small for gestational age (i.e. their birth weights were less than 10^{th} centile for gestational age). This

agrees with the general consensus that high prevalence of low-birth weight due to IUGR occurs more frequently in multiple pregnancy [2]. The same was found in the studies done in Ghana[7] and England [39].

In this study, among multiple-birth newborns whom were small for gestation age, about 6% were of very–low birth weights (that is less than the 3rd centile for gestational age), but no one in the control group being in this category.

The percentage of twins weighing less than 1.5kg was about quarter that found in another English study [36].

Participation of preterm labour also was dramatic. About 40% of multiple-birth newborns were delivered before term (i.e. less than 37weeks gestation), compared to only 4% in singletons. Those who were delivered before the 32weeks gestation contribute to a significant proportion compared to singletons. This was also found in general population[1] .

The median gestational ages for twins and triplets were also compatible with those found in England [39] and

USA [40].

In fact, such a high number of LBW and preterm deliveries had led to a serious strain in NICUs , which were limited in their quality and quantity .

Multiple-birth newborn infants are at greater risk of birth asphyxia than singletons [49]. This susceptibility to asphyxia was also confirmed in this study as also found in Bulgaria [46].

About 6% of multiple-birth newborns were affected compared to 1.4% of singletons. The participation of twins alone was 4% which was approximately as twice as that found in a Nigerian study [6].

However, in this study developing asphyxia was not affected by birth order, or as found in study done in United States of America [45-47], and elsewhere. [53] Another study revealed that the risk of neonatal death, especially for term infants with asphyxia-related deaths, is increased for the 2nd twins who are delivered by C/S after vaginal delivery of the first twins. [51]

Among the 149 multiple-birth newborns, only 1

(1.4%) was delivered congenitally malformed, but no one in the control group .

In this study congenital anomalies were not found to be increased in twins and higher order multiple-birth newborns. This agrees with the general consensus that prevalence of congenital malformations in multiple-birth newborns is not in excess of that singletons. But incompatible with studies done in Bulgaria [46] and elsewhere [81] , where congenital malformations were associated with multiple pregnancy .

The link between gestational age , which in turn is influenced by twining , and the development of RDS in the first versus second twins was not found in this study. P = 0.43 Fig. 4 . This was different from study done in U.S.A which showed that the second twins were more likely to be intubated , have RDS, and need resuscitation [47] . Although a study which compared the outcome of the second twin with that of the first twin , showed that the increased risk of the second twin to RDS is related to malpresention rather than birth order [45] .

The relationship between birth weight and early neonatal death (death in the first week of life) is well established in this study (Tab.9) in which 8.2% of the first born infants , 16.4% of the second born infants , and only 1.4% of singletons whose birth weights were less than 1.5 kg had died .This agrees with the study which showed that twins with very low birth weights (less than 1.5kg) , comprised 69% of all perinatal deaths [36].

A significant number of multiple birth was left in the NICU by the end of the first week , compared to only one in the control group , PV = 0.0009 . Also by the end of the first week 20(13%) of multiple births had died compare to only one in the control group, PV = 0.0003 ,with an over all mortality rate of 94.6 / 1000 , Tab. 10. A higher PNMR were also found in University of Ilorin Teaching Hospital , Nigeria [37] , University of Maiduguri Teaching Hospital , and else where [36]. Also in study done in U.S.A (1980-1999) , the result showed that multiple births experienced grater declines in infants mortality rate [4] .

Occurrence of physiological jaundice comprised

considerable participation, in both multiple birth infants and singletons but multiple birth were not at specific risk.

More than 7.5% of multiple-birth newborn infants were affected by neonatal sepsis compared to 4% in singletons, but again multiple births were not at specific risk . Indepth and extensive neonatal studies aimed at useful approach that allow for exploration of relationship between twinning and both physiological jaundice and neonatal sepsis were needed.

As far as the racial groups of the mother were concerned, there is no abundant evidence to suggest that multiple pregnancies are related to ethnic group. This finding is different from the results obtained from Africa and Asia [1], and American studies[3,4].

This may be attributed, in part , to overlapping between eastern , western , central , northern and southern tribes, leading to overlapping of racial groups (you can not put Rizegatt tribe in west of Sudan as a separate entity from Shygya tribe in north of Sudan if you want to classify them as Negros and non-Negros if the international opinion about Sudanese is considered , i.e. They are considered as

approximately one ethnic group).

Females with higher parity have a higher chance of multiple pregnancy than those is lower parity. [1]

A significant number of the females who gave birth to multiple newborns were grandmultiparous. This relationship between rising parity and multiple pregnancy was found in Nigeria [6] , Ghana [7] , and Sudan [26].

Multiple pregnancy is strongly associated with maternal age. In this study about half of the mothers who gave delivery to multiple-birth newborns were above 30 years of age compared to 17% of those who gave delivery to singletons . A similar correlation was found in USA [4] , Nigeria [6] , Netherland [9] and Japan [10] , although study done by Dr. N. Elsadig in Sudan revealed that there was no effect of maternal age on multiple pregnancy [26].

Family history of multiple pregnancies is well associated with multiple pregnancy [1]. In this study the challenge of the relationship between multiple pregnancy and family history revealed that most (83.6%) of those who gave birth to multiple newborns had a family history of multiple

pregnancy, compared to 45% of those who gave birth to singletons .This is similar to findings of studies done in Nigeria, Netherlands [24] and Sudan. [26]

Forty-five percent of mothers who gave birth to singletons and who had a family history of multiple pregnancy is a large percentage , but I think these relatives of ladies who gave birth to singletons might be exposed to the same risk factors as the relatives of those who had multiple pregnancies .

The relationship between multiple pregnancy and the use of fertility drugs (hormones) exists [15,16]. In this study the only women who used ovulation enhancing hormone, was in the control group . Although the study which assessed neonatal outcome after ovarian stimulation showed that twining and triplets rates were higher than those of singletons.[20] Again it is different from the results obtained from Japanese study [10] , and study done in Netherlands. [19]

This paradoxical finding may be due to the fact that the use of these drugs is not common in Sudan, and again it may be attributed to the scarcity of the number of the population

examined.

The past history of multiple pregnancy had no dramatic effect in the occurrence of multiple pregnancy. Here 2.8% of the women who gave births to multiple-newborns had a past history of multiple pregnancy, and only half of this percentage were those who gave birth to singletons .

A large proportion (12.3%) of the women who gave birth to multiple newborns had delivered abdominally, compared to 2.8% of the control group. This may expose both newborn infants and their mothers to the risk of anaesthesia, sedation , or even death .

4.1 CONCLUSION

- Multiple-birth infants complications had been known

since the dawn of history, and up to now their solution are beyond reach in Sudan.

- Low-birth weight was a major problem in multiple-birth newborns. An average of 43% of them were small for gestational age with 2% were very small for gestational age. In singletons 8.2% had low-birth weights.
- Preterm births also was encountered in a large percentage of multiple-birth newborns. Forty per cent of them were delivered before term and approximately half of these were delivered before 32 weeks of gestation. On the other hand, 4.1% of singletons were preterm (3rd of them were delivered before 32 week gestation).
- About 54% of multiple birth newborns were males and 46% were females. There were 17 pairs of like-sex. In singletons 58.9% were males and 41.1% were females.
- Only one newborn was affected by congenital malformation, and this was found in singletons only.
- Multiple-birth infants follow-up had revealed that by the end of the first week of age 13.4% were died ,10.7% were left in NICU and the remaining 75.9% were discharged

home ,while that of singletons had revealed 1.4% , 1.4% and 97.2% respectively .

- Eight percent of multiple-birth infants were asphyxiated compared to 1.4% in singletons.
- About 13.4% of multiple-birth infants had developed RDS. All of them were less than 32weeks gestation. Only one (1.4%) in the control group had developed RDS and his gestational age was less than 32 weeks .
- About 7.4% of multiple-birth infants had developed neonatal sepsis ,compared to 4% in singletons .
- Physiological jaundice had affected 6% of multiple-birth infants and 4.1% of singletons .
- A bout 39.7% of the mothers who gave birth to multiple-birth infants were northern, 1.4% were eastern, 20.5% were western, 11% were southern and 27.4% were central. The corresponding percentages in the control group were 50.7%, 1.4%, 19.2%, 5.5% and 23.3% respectively.
- About 34.3% of women who gave births to twins or triplets were grandmultiprous and 23.3% of them were

primigravidae, compared to 10.9% and 50%, respectively for those who gave births to singletons .

- Multiple pregnancy was strongly influenced by maternal age. Half of the mothers who had multiple pregnancies were above 30 years of age compared to 17.8% in those in the control group.
- About 83.6% of the mothers who had multiple pregnancies and 45% in the control had a family history of similar events .
- Only one woman used ovulation enhancing-hormone, and surprisingly she was found in the control group.
- Nine percent of the women who gave multiple-births had delivered abdominally compared to 2.8% in the control group.

4.2 RECOMMENDATIONS

- Mothers' counseling about family planning (spacing) and

the effect of increased parity in multiple pregnancy, to reduce parity, using all types of media.

- Mothers' counseling about the effect of the advanced maternal age on multiple pregnancies, and early females marriage should be encouraged, again using all types of media .
- Prevention of preterm delivery of multiple–birth infants, whenever neonatal risks would overweigh those of the mothers.
- In order to inform health care planning, continuous monitoring of trends in multiple-birth and their mortalities and morbidities is needed.
- Attendance of multiple-birth deliveries by paediatrics registrars, with strong anticipation and aggressive intrapartum management of the complications is essential in all such deliveries.
- Further studies in the relationship between multiple pregnancy and racial group, past history of multiple pregnancy and the use of ovulation-enhancing drugs, on one hand, and the relationship between multiple-births and RDS, physiologic jaundice and neonatal sepsis on the other hand are recommended.
- If preterm delivery is inevitable, steroid in a form of dexamethazone must be given for the pregnant lady 48 hours before delivery.

REFERENCES

(1) Jeorge S, editorial. Multiple pregnancy. Obstetrics by Ten Teachers, 17th ed. Bombay: Ajanta Offset and Packaging Ltd., 2000.p.187-91.

(2) Beischer NA, Mackay EV, Colditz PB, editorials. Multiple pregnancy. Obstetrics and the Newborn: An Illustrated Textbook. Philadeophia: W. B. Saunders Company; 1997.p.258-273.

(3) Smith-Levitin M, Skupski DW, Chervenak FA. Multifetal pregnancies: epidemiology, clinical characteristics and management. Medicine of the fetus and newborn. Paediatric 2005; 70: 33-40.

(4) Russell RB, Petrini JR, Damus K, Mattison DR, Schwarz RH. The changing epidemiology of multiple births in the United States. Obstet Gynaecol 2003; 101(1): 129-35.

(5) Barbara J, Stoll W. The fetus and the neonatal infant. In: Richard EB, Robert MK, Hal BJ, editors. Nelson Text Book of Pediatrics, 16th ed. Philadelphia: Saunders Company; 2000.p.451-538.

(6) Aisien AO, Olarewaju RS, Imade GE. Twins in Jos Nigeria: a seven-year retrospective study. Med Sci Monit 2000; 6(5): 945-50.

(7) Nkyekyer K. Twin and singleton births in Ghana: a case control study. Twin Res 2002; 5(4): 265-69.

(8) Savona-Ventura C, Grech EC. Multiple pregnancies in the Maltese population. Int J Gynaecol Obstet 1988; 26(1): 41-50.

(9) Theunissen RP, Zwertbroek WM, Huisjes AJ, Kanhai HH, Briomse HW, Merkus HM. Multiple birth prevalence in the Netherlands. Impact of maternal age and assisted reproductive techniques. J Reprod Med 1998 Mar; 43(3): 173-9.

(10) Imaizumi Y, Nonaka K. Rising trizygotic triplet rates in Japan, 1975-1994. Acta Genet Med Gemellol Roma 1997; 46(2): 87-98.

(11) Bertranpetit J, Marin A. Demographic parameters and twining: a study in Catalonia, Spain. In: Acta Genet Med Gemoll Roma 1988; 37(2): 127-35.

(12) Doyle P. The outcome of multiple pregnancy. Hum Reprod 1996; 11(4): 110-17.

(13) Taffeta SM. Health and demographic characteristics of twin births: United States, 1988. Vital Hlth Statist 1992; 21: 50.

(14) Kiely JL, Kleinman JC, Kiely M. Triplets and higher order multiple births: time trends and infant mortality. AJDC 1992; 146: 862-68.

(15) Keith LG, Papiernik E, Luke B. The cost of multiple pregnancy. Int J Gynaecol Obstet 1991; 36: 104-14.

(16) Botting BJ, Davies IM, MacFarlane AJ. Recent trends in the incidence of multiple births and associated mortality. Arch Dis Child 1987; 62: 941-50.

(17) Alvarez M, Berkowitz R. Multifetal gestation. Clin Obstet Gynaecol 1990; 33: 79-87.

(18) Murphy M, Seagroatt V. Twins peaks, extramarital conceptions, and virgin births: is there a connection?. Arch Dis Child 1992; 67: 189-91.

(19) Steegers-Theunissen RP, Zwertbroek WM, Huisjes AJ, Kanhai HH, Bruinse HW, Merkus HM. Multiple birth prevalence in the Netherlands. Impact of maternal age and assisted reproductive techniques. J Reprod Med 1998; 43(3): 173-79.

(20) Kallen B, Olausson PO, Nygren KG. Neonatal outcome in pregnancies from ovarian stimulation. Obstet Gynaecol 2002; 100(3): 414-19.

(21) Meredith A, Laura A, Joyce A, Jeng G, Macaluso M. Trends in multiple births conceived using assisted reproductive technology, United States, 1997-2000. Va Law Rev 1983 Apr; 69(3): 405-64.

(22) Lambalk CB, VanHoff M. natural versus induced twinning and pregnancy outcome: a Dutch nationwide survey of primiparous dizygotic twin deliveries. Fertil Steril 2001; 75: 731-36.

(23) Philip N, editorial. Twins and higher multiple gestations. Obstetrics by Ten Teachers;18th ed. Philadelphia: Saunders; 2000.p.146.

(24) Eriksson AW. Twinning in families of triplets. Acta Genet Med Gemellol Roma 1990; 39(3): 279-93.

(25) Sherman SL, Tunner G, Sheffield L, Lating S, Robinson H. Investigation of the rate in families with the fragile x syndrome. Am J Med Genet 1988; 30(1-2): 625-31.

(26) Elsadig N. The incidence of multiple pregnancy in Soba Hospital. MD Thesis. University of Khartoum; Sudan: 1997.p. 45-9.

(27) Adam IA. The outcome of the second versus the first twin. MD Thesis. University of Khartoum; Sudan: 1998.p. 27-33.

(28) Ibrahim SA. A cohort study of risk factors of perinatal mortality. MD Thesis. University of Khartoum; Sudan: 1994.p.66-70.

(29) Yousif G. Preterm births: incidence of specific risk factors at Soba University Hospital. MD Thesis. University of Khartoum; Sudan: 1996.p.32.

(30) Salwa AG. The factors associated with low birth weight in Omdurman Maternity Hospital. MPEH Thesis. University of Khartoum; Sudan:2002.p. 43.

(31) Ahmed NM. Maternal and childhealth care. MPEH Thesis. University of Khartoum; Sudan:1987.p. 65-67.

(32) Fisk NM. Multiple pregnancy. In: Keith D, editor. Dewhurst's Textbook of Obstetric and Gynaecology for Postgraduate, 6th ed. Hong Kong: MPG books Ltd; 1999.p.298.

(33) George C. Perinatal outcome and referred age. Paediatrics 1975; 56(6): 160.

(34) Jolly H, Levene MI. Disease of children. Paediatrics, 5th ed. Oxford: Blackwell Scientific Publications; 1985.p.31.

(35) Robert MK. Fetal and neonatal medicine. In: Nelson J, editor. Essential of Paediatrics, 4th ed. Philadelphia: Sounder's Company; 2002.p.179.

(36) Gliniannaia SV, Rankin J, Renwick M. Time trends in twin perinatal mortality in northern England, 1982-94. Northern region perinatal mortality survey steering group. Twin Res 1998; 1(4): 189-95.

(37) Fakeye O. Breech births in twin pregnancy; an analysis of Apgar score and perinatal mortality from a Nigerian sample. Int J Gynaecol Obstet 1988; 27(1): 11-6.

(38) Wessel J, Schmidt-Gollwitzer K. Intrauterine death of a single fetus in twin pregnancies. J Perinat Med 1988; 16(5-6): 467-76.

(39) Santema JG, Bourdrez P, Wallenburg HC. Maternal and perinatal complication in triplet compared with twin pregnancy. Eur J Gynaecol Obstet Reprod Biol 1995; 60(2): 143-47.

(40) Kaufman GE, Malone FD, Harvey-Wilkes KB, Chelmow D, Penzias AS, D'Alton ME. Neonatal morbidity and mortality associated with triplet pregnancy. Gynaecol Obstet 1998; 91(3): 342-48.

(41) Fisk NM, Bryan E. Routine prenatal determination of chorionicity in multiple gestation: a plea to the obstetrician. Br J Gynaecol Obstet 1993; 100: 975-77.

(42) Moore TR, Gale S, Benirschke K. Perinatal outcome of 49 pregnancies complicated by cardiac twinning. Am J Gynaecol Obstet 1990; 163: 907-12.

(43) Ville Y, Hecher K, Gagnan A, Sebine N, Hyett J, Nicoloides K. Endoscopic laser coagulation in the management of severe twin transfusion syndrome. Br J Gynaecol Obstet 1998; 105: 446-53.

(44) Wen SW, Fung KF, Oppenheimer L. Neonatal mortality in second twin according to cause of death, gestational age, and mode of delivery. Am J Obstet Gynaecol 2004; 191: 778-83.

(45) Arnold C, Mclean FH, Karmer-Usher RH. Respiratory distress syndrome in second born versus first-born twin. A maternal case control analysis. N Engl J Med 1987; 317(18): 1121-125.

(46) Vkrilova L, Kalaidzhieva M, Kolev D, Dacheva S, Purvanova Z. The structure and analysis of neonatal mortality in twins in 1991-1995 at the state university hospital maternity home, Sofia. Akush Ginekol Sofia 1997; 36(2): 5-8.

(47) Prins RP. The second born twins: can we improve outcome?. Am J Obstet Gynaecol 1994; 170 (6): 1649-656.

(48) Jolly H, Levene MI. Asphysia. In: Behrman RE, Kliegman RM, Arvin AM, eds. Disease of Children, 5th ed. Oxford: Blackwell's Scientific Publications; 1985.p.90.

(49) American Academy of Pediatrics , American Collage of Obstetricians and Gynecologists . Guidelines for Perinatal Care, 4th ed. New York : EIK Grove Village,IL,AAP; 1997.p.155-60 .

(50) Ghai V, Vidyasagar D. Morbidity and mortality factors in twins An epidemiologic approach. Clin Perinatal 1988; 15(1): 123-40.

(51) Wen SW; Fung KF; Oppenheimer L; Demissie K; Yang Q; Walker M Neonatal mortality in second twin according to cause of death, gestational age, and mode of delivery. Am J Obstet Gynecol 2004 Sep;191(3):778-83.

(52) Glinianaia SV, Pharoah P, Sturgiss SN. Comparative trends in cause-specific fetal and neonatal mortality in twin and singleton births in the North of England, 1982-1994. Br J Obstet Gynaecol 2000; 107(4): 452-60.

(53) Andrews WW, Levenok J, Sherman MI. Elective hospitalization in the management of twin pregnancies. Obstet Gynaecol J 1991; 77: 826.

(54) Yokohama Y, Shimizu T, Hayakawa K. Prevalence of cerebral palsy in twins, triplets and quadruplets. Int J Epidemiol 1995; 24(5): 943-48.

(55) Carl E, Hunt S. Sudden infant death syndrome. In: Richard EB, Robert MK, Hal BJ, editors. Nelson Text Book of Paediatrics, 16th ed. Philadelphia: Saunders Company; 2000.p. 2139.

(56) Cross T, Lewis S. Sudden infant death syndrome. In: Tolly H, Levene MI. Disease of children, 5th ed. Oxford: Blackwell Scientific Publications; 1985.p. 632.

(57) Arsenault PS. Maternal and antenatal factors in the risk of sudden infant deaths syndrome. Am J Epidemiol 1980; 3: 278-84.

(58) Kraus JP. Methodologic considerations in the search for risk factors unique to sudden infant deaths syndrome. In: Tildon JT, Roeder LM, Steinschneider A, editors. Sudden Infant Death Syndrome, 5th ed. New York, NY: Academic Press; 1983.p. 43-58.

(59) Rintahaka PJ. Sudden infant death syndrome in Finland in 1969-1980. Nation Board Hlth Finland 1985; 3: 53.

(60) Fleming PJ. Environment of infant during sleep and risk of the sudden infant death syndrome; results of 1993-5 case-control study for confidential enquiry into stillbirths and deaths in infancy. BMJ 1996;313:191-5.

(61) Guntheroth MD, Spiers PS. Sleeping prone and the risk of sudden infant death syndrome. J Am Med Assoc 1992; 267: 2359-62.

(62) Confidential Enquiry into Stillbirths and Deaths in Infancy 1 Jan-31 December 1994. London: Department

of Health, 1996. (Type IV evidence - statistical information) http://www.bmj.com/cgi/content/full/313/7051/195

(63) Blair PS, Fleming PJ, Bensley D. Smoking and the sudden infant death syndrome. BMJ 1996;313:195-8.

(64) Poets CF, Schlaud M, Kleemann QJ *et al.* Sudden infant death and maternal cigarette smoking: results from the Lower Saxony Perinatal Working Group. Eur J Paediatr 1995;154:326-9.

(65) Confidential Enquiry into Stillbirths and Deaths in Infancy. 1 January - 31 December 1994. London. http://www.bmj.com/cgi/content/full/313/7051/195

(66) Adelson L, Kinney ER. Sudden and unexpected death in infancy and childhood. Pediatrics 1956; 17: 663-99.

(67) Coe JI, Hartman EE. Sudden unexpected death in infancy. J Pediatr 1960; 56: 786-94.

(68) Kraus JF, Borhani NO. Post-neonatal sudden unexplained death in California: A cohort study. Am J Epidemiol 1972; 95: 497-510.

(69) Valdes-Dapena M. Sudden unexplained infant death, 1970 through 1975: an evolution in understanding. US Department

of Health, education and Welfare publication (HAS) 80-5255. Philadelphia: Government Printing Office; 1980.p. 1-25.

(70) Spiers PS. Estimated rates of concordance for the sudden infant death syndrome in twins. Am J Epidemiol 1974; 100: 1-6.

(71) Susan-Beal MD. Sudden infant death syndrome in twins. J Pediatr 1989; 84(6): 1038-43.

(72) Rise M, Weiler G. Epidemiology andmorphology of sudden death in infancy in twins and siblings. Beitr Gericht Med 1991; 49: 29-32.

(73) Plat MJ, Pharoah PO. The epidemiology of sudden infant death syndrome. Arch Dis Child 2003; 88(1): 27-9.

(74) Jolly H, Levene MI. Diseases of children: a book of paediatrics, 8th ed. Oxford: Blackwell Scientific Publications; 1985.p. 128.

(75) Burroughs N, Leape LL. Laryngotracheoesophageal cleft: report of a case successfully treated and review of the literature. Pediatrics 1974; 53: 516.

(76) Esterly JR. Anatomic malformations of the lower respiratory tract. Birth Defect 1974; 10(4): 217.

(77) Beazer R, Freeland AP, Robertson NRC. Laryngotracheoesophageal cleft. Arch Dis Child 1973; 48: 912.

(78) Fuzesi K, Young DG. Congenital Laryngotracheoesophageal cleft. J Pediatr Surg 1976; 11: 933.

(79) Maltz DL, Nadas AS. A genesis of the lung, presentation of eight new cases and review of the literature. Pediatrics 1968; 42: 175.

(80) Booth JB, Jerry CL. Unilateral pulmonary agenesis. Arch Dis Child 1967; 42: 361.

(81) Carson BJ, Towers CV. Multiple gestation complicated by death of one fetus. Obstet Gynaecol J 1989; 685-89.

(82) Fisk NM, Borrell A, Hubinot C, Tannirandorn T, Nicolini V, Rodeck CH. Fetofetal transfusion syndrome: do the neonatal criteria apply in utero?. Arch Dis Child 1990; 65(7 spec no): 657-61.

(83) Entezami M, Runkel S, Becker R, Weitzel HK, Arabin B. Feto-feto-fetal triple transfusion syndrome (FFFTTS). J Matern Fetal Med 1997; 6(6): 334-37.

(84) Sohn C, Wallwiener D, Kurek R, Hahn U, Schiesser M, Bastert G. Treatment of the twin-twin transfusion syndrome: initial experience using laser induced interstitial therapy. Fetal Diag Ther 1996; 11(6): 390-97.

(85) Chang DY, Chang TY, Chen RJ, Chen CK, Chang WF, Huang SC. Triple pregnancy complicated by intrauterine fetal death of co-joined twins from an umbilical cord accident of an arcadias. A case report. J Reprod Med 1996; 41(6): 459-62.

(86) Dommergues M, Mandelbort L, Delezoide AL, Aubry MC, Fermont L, Caputo-Mahieu D, Dumez Y. Twin-to-twin transfusion syndrome. Selective feticide by embolication of the hydropic fetus. Fetal Diag Ther 1995; 10(1): 26-31.

(87) Pierce MI. Leukemia in the newborn infant. J Pediatr 1959; 54: 691-706.

(88) Zussman WV, Khan A, Shayesteh P. Congenital leukemia. Cancer 1967; 20: 1227-233.

(89) Hawthrorne HC, Nelson JS, Witzleben CL. Blanching subcutaneous nodules in neonatal neuroblastoma. J Pediatr 1970; 77: 297-300.

(90) Brough AJ, Jones D, Page RH. Dermal erythropoiesis in neonatal infants: a manifestation of intrauterine viral disease. Pediatrics 1967; 40: 627-35.

(91) Aryle JC, Zone JJ. Dermal erythropoiesis in neonate. Arch Dermatol 1981; 117: 792-94.

(92) Bhargava I, Chakravavty A. Vascular anastomoses in twin placentas and their recognition. Acta Anat 1975; 93: 471-80.

(93) Rausen AR, Seki W, Strauss L. Twin transfusion syndrome. J Pediatr 1965; 66: 613-28.

(94) Popoff L, Popoff N. L'hemopoiese acutance an cours de la vie intrauterine. Ann Dermatol Venereal 1958; 85: 157-67.

(95) Ortonne JP, Jenne R, Perrot H. Myeloid metaplasia of the skin in two patients suffering from primary myelofibrosis. Arch Dermatol 1977; 113: 1459.

Table (1): Birth distribution according to hospital

(n = 222)

Hospital	Number of birth			Total
	Singletons (control)	Twins	Triplets	
OMH	44	82	9	135
KTH	19	38	0	57
KNTH	10	20	0	30

Table (2): weight distribution in multiple-birth versus singleton newborns

	0.5-0.99	1-1.49	1.5-1.99	2-2.49	2.5-2.99	3-3.49	3.5-3.99	4-4.49	Total	p. value
1st	4(5.5%)	10(13.6%)	13(17.82%)	27(37%)	16(21.9%)	2(2.8%)	1(1.4%)		73	0.00001
Control		1(1.4%)	2(2.8%)	4(5.5%)	23(13.5%)	39(53.2%)	2(2.8%)	2(2.8%)	73	
2nd	6(8.2%)	8(11%)	11(15%)	28(38.4%)	16(21.9%)	4(5.5%)			73	0.00001
Control		1(1.4%)	2(2.8%)	4(2.8%)	23(31.5%)	39(53.2%)	2(2.8%)	2(2.8%)	73	
3rd		1(33.3%)	2(66.7%)						3	0.00002
Control		1(1.4%)	2(2.8%)	4(5.5%)	23(31.5%)	39(53.2%)	2(2.8%)	2(2.8%)	73	

Table (3) : Birth weight centiles in multiple-birth and singleton newborns

	<3rd	3rd -<10th	10th -<25th	25th -<50th	50th -<75th	75th-<90th	>90th	Total	p.value
1 st	1(1.4%)	31(42.4%)	13(17.8%)	28(38.42%)				73	0.000
Control		6(8.2%)	7(9.6%)	12(16.4%)	44(59.8%)	2(2.8%)	2(2.8%)	73	
2 nd	2(2.8%)	29(39.7%)	7(9.6%)	35(47.9%)				73	
Control		6(8.2%)	7(9.6%)	12(16.4%)	44(59.8%)	2(2.8%)	2(2.8%)	73	0.000
3 rd	1(33.3%)	1(33.3%)	1(33.3%)					3	
Control		6(8.2%)	7(9.6%)	12(16.4%)	44(59.8%)	2(2.8%)	2(2.8%)	73	0.3

Table (4): 1 minute Apgar score in multiple-birth and singleton newborns

	0-3	4	5-7	8-10	Total	p.value
1 st	2(2.8%)	8(11%)	25(34.2%)	38(52%)	73	0.0002
Control		2(2.8%)	9(12.3%)	62(84.9%)	73	
2 nd	4(5.5%)	22(30.2%)	38(52%)	9(12.3%)	73	0.0001
Control		2(2.8%)	9(12.3%)	62(84.9%)	73	
3 rd	1(33.3%)	1(33.3%)	1(33.3%)		3	0.00014
Control		2(2.8%)	9(12.3%)	62(84.9%)	73	

Table (5): 5 minutes Apgar score in multiple-birth and singleton

	0-3	4	5-7	8-10	Total	p.value
1 st	1(1.4%)		13(17.8%)	59(80.8%)	73	0.17
Control		1(1.4%)	6(8.2%)	66(90.4%)	73	
2 nd	2(2.8%)	2(2.8%)	15(20.5%)	54(73.9%)	73	0.06
Control		1(1.4%)	6(8.2%)	66(90.4%)	73	
3 rd			1(33.3%)	2(66.7%)	3	0.33
Control		1(1.4%)	6(8.2%))	66(90.4%)	73	

Table (6): Asphyxia to gestational age , 1st born infant vs 2nd born infants

	28-32 wks	33-36wks	37-42wks
1st	1(1.4%)	1(1.4%)	0
2nd	4(5.5%)	1(1.4%)	1(1.4%)
Total	5(6.9%)	2(2.8%)	1(1.4%)

Table (7):Relationship between neonatal sepsis and gestational age in multiple-birth and singleton newborns

	28-32 wks	33-36 wks	Total	p.value
1st	2(2.82%)	2(2.8 %)	4(5.6%)	0.74
Control	2(2.8%)	1(1.4%)	3(4.1%)	
2nd	3(4.1%)	4(5.5%)	7(9.6%)	0.512
Control	2(2.08%)	1(1.4%)	3(4.1%)	

Table (8):Relationship between physiologic jaundice and birth weight in multiple-birth and singleton newborns

	1-1.49kg	1.5-1.99kg	2-2.49kg	Total	P.value
1st	1(1.4%)	2(2.8 %)	1(1.4%)	4(5.6%)	0.64
Control	1(1.4%)	2(2.8 %)		3(4.1%)	
2nd	2(2.8 %)	3(4.1%)		5(6.9%)	0.57
Control	1(1.4%)	2(2.8%)		3(4.1%)	

Table (9):Relationship between birth weight and mortality in multiple-birth and singleton newborns

	0.5-0.99kg	1-1.49kg	1.5-1.99kg	Total	P.value
1st	5(6.8%)	1(1.4%)	0	6(8.2%)	0.08
Control	1(1.4%)			1(1.4%)	
2nd	11(15 %)	1(1.4%)	1(1.4%)	13(17.8%)	0.039
Control	1(1.4%)			1(1.4%)	
3rd	1(33.3%)			1(33.3%)	0.15
Control	1(1.4%)			1(1.4%)	

Table (10): The outcome of multiple-birth and singleton newborns by the end of the first week

	Discharged	Still in NICU	Died	Total	P.value
1st	57(78.1%)	10(13.7%)	6(8.2%)	73	0.001
Control	71(97.2%)	1(1.4%)	1(1.4%)	73	
2nd	54(74%)	6(8.2%)	13(17.8%)	73	0.0003
Control	71(97.2%)	1(1.4%)	1(1.4%)	73	
3rd	2(66.7%)		1(33.3%)	3	0.0003
Control	71(97.2%)	1(1.4%)	1(1.4%)	73	

Table (11): Distribution of ethnic group (Case &control)

	North		East		West		South		Centre	
	No.	%	No.	%	No.	%	No.	%	No.	%
Case	29	39.7	1	1.4	15	20.5	8	11	20	27.4
Control	37	50.7	1	1.4	14	19.2	4	5.5	17	23.3
Total	66	45.2	2	1.4	29	19.9	12	8.1	37	25.4

P= 0.630

Table (12): Parity (Case &control)

	GROUP			
	CASE		CONTROL	
No.of birth	No .	%	No.	%
I	17	23.3	36	49.3
II	10	13.7	13	17.9
III	9	12.3	12	16.4
IV	12	16.4	4	5.5
V	12	16.4	6	8.2
VI	13	17.9	2	2.7
Total	73	100	73	100

P= 0.001

Table (13): Maternal age distribution (Case &control)

	GROUP			
	CASE		CONTROL	
Age(Yrs)	No .	%	No.	%
15-19	2	2.7	12	16.4
20-24	19	26	28	38.3
25-29	16	21.9	20	27.3
30-34	22	30.2	9	12.3
35-39	12	16.4	3	4.1
40-44	1	1.4	1	1.4
45-49	1	1.4		
Total	73	100	73	100

P= 0.002

Figure 1 Birth weight to gestational age (multiple – birth infants & control)

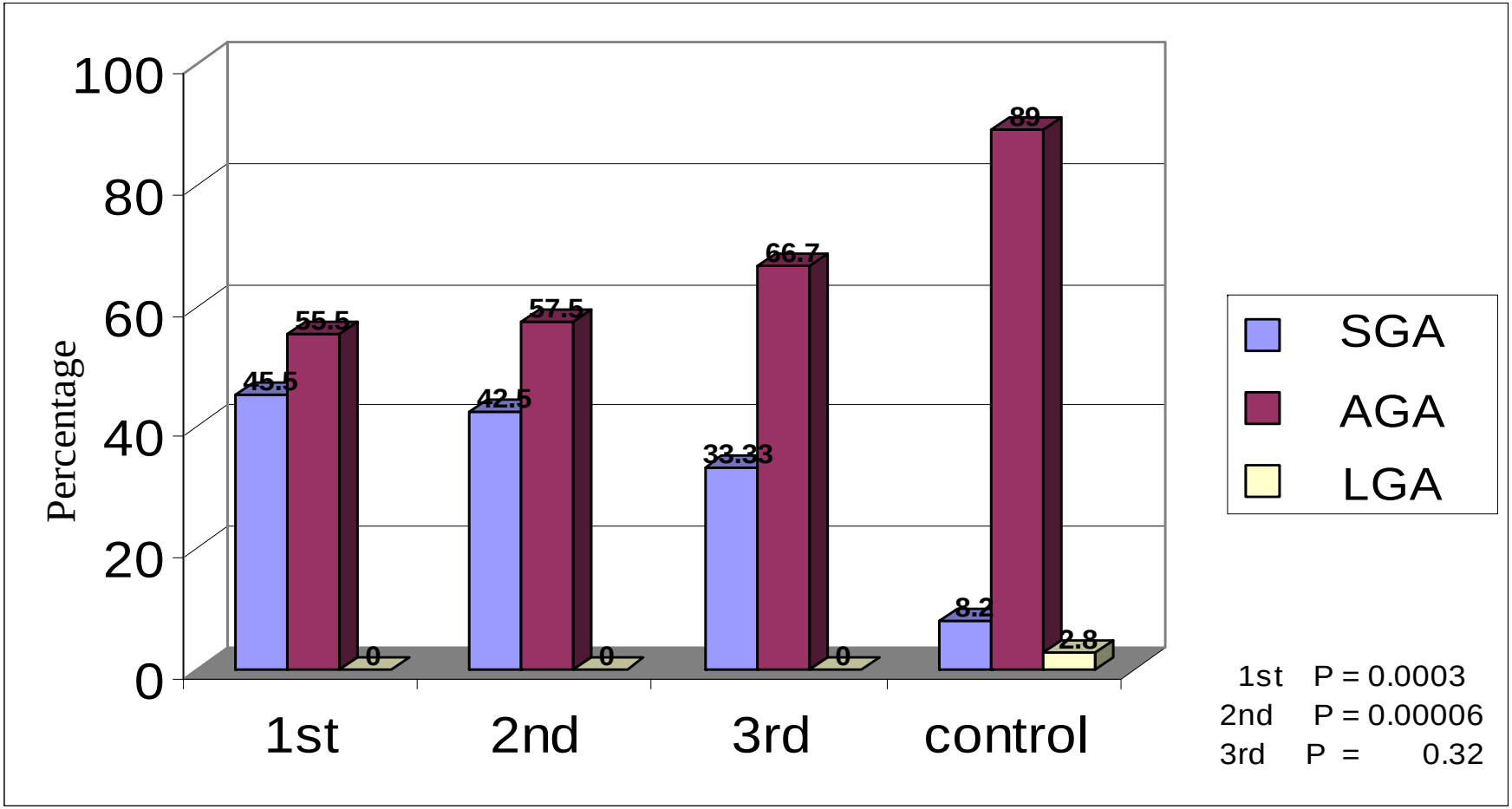


Figure 2: Gestational age in multiple – birth newborns and singletons

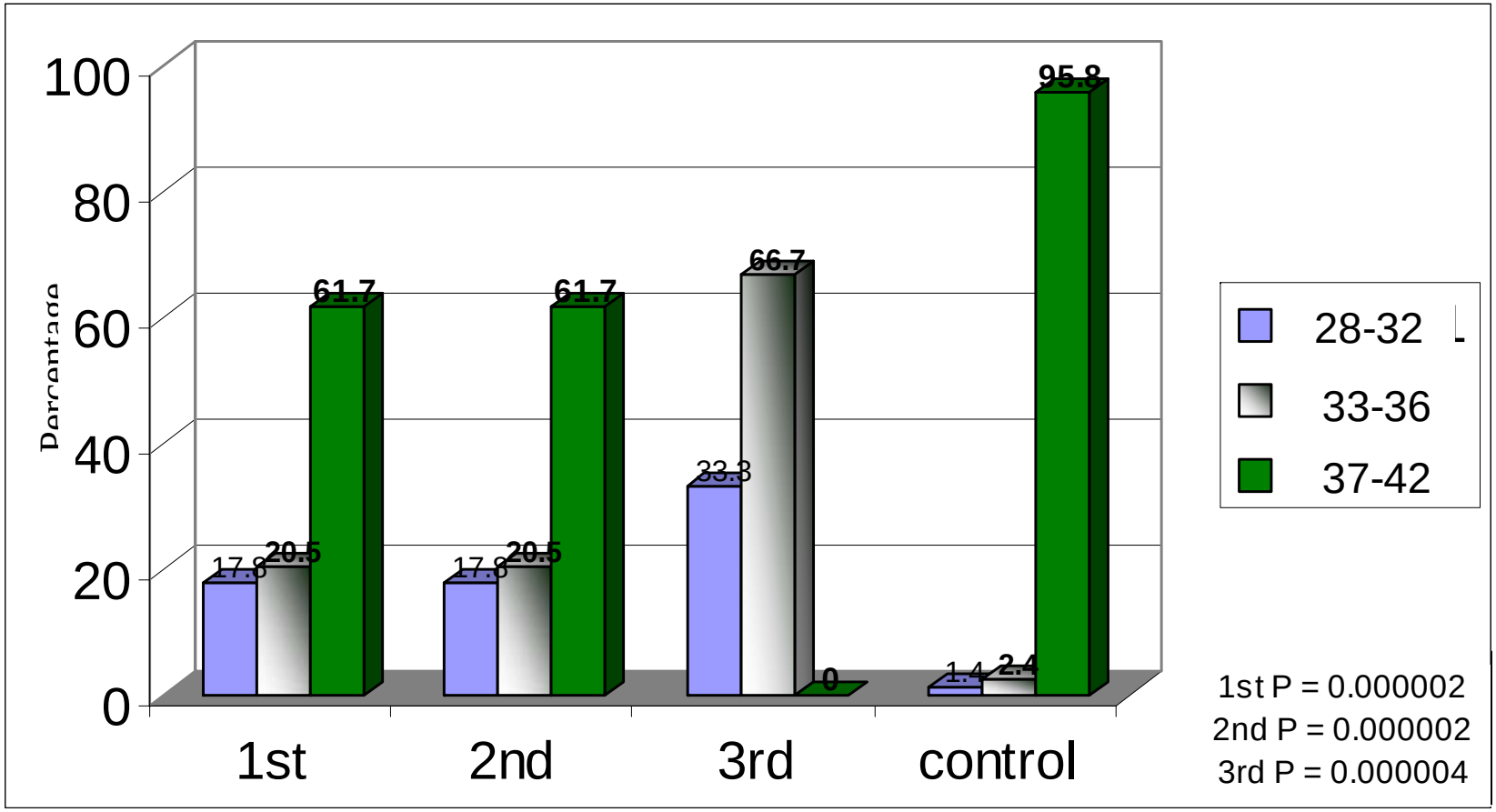


Figure 3 : Sex percentage

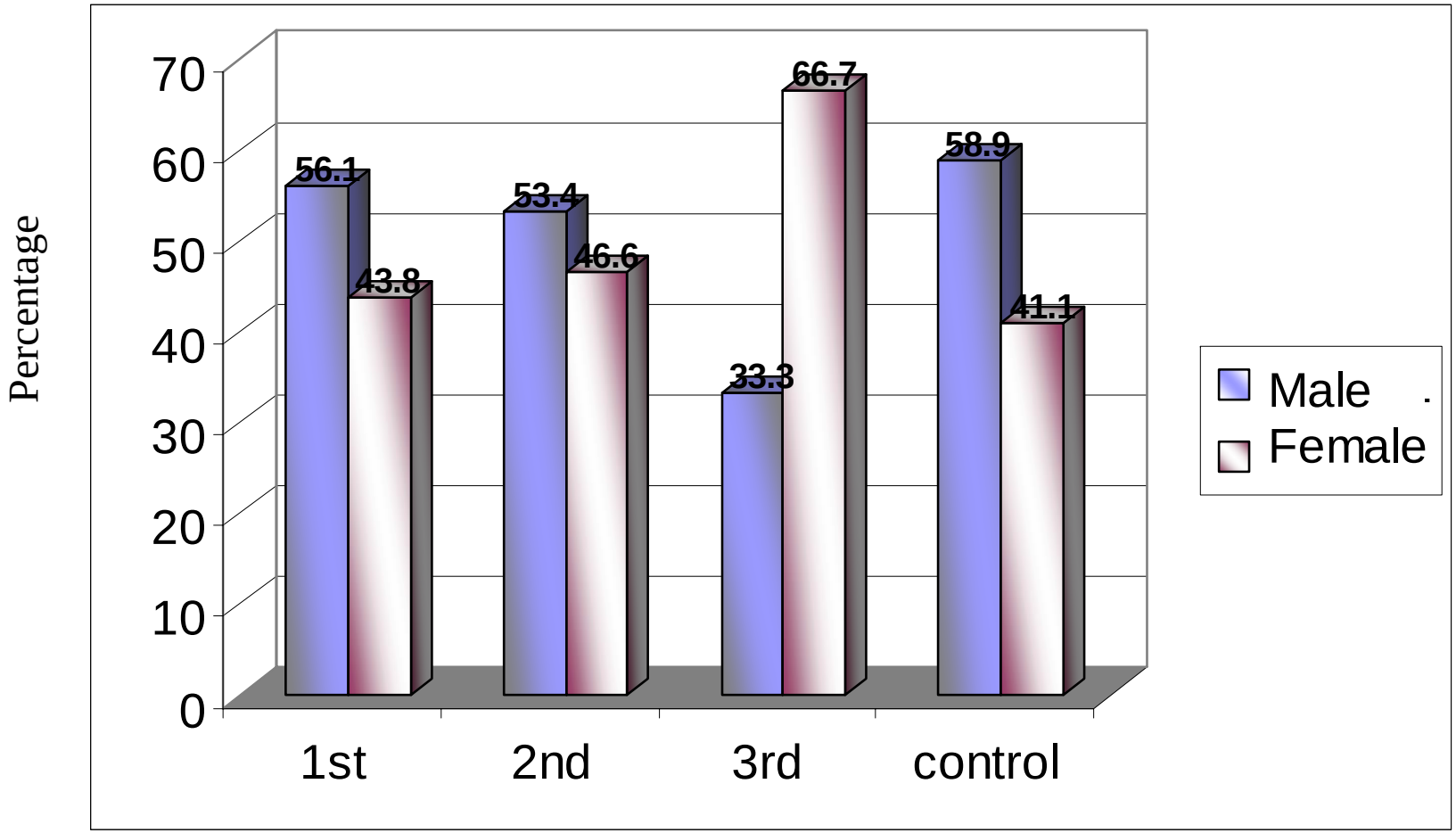


Figure 4: RDS in relation to gestational age (1st , 2nd & control)

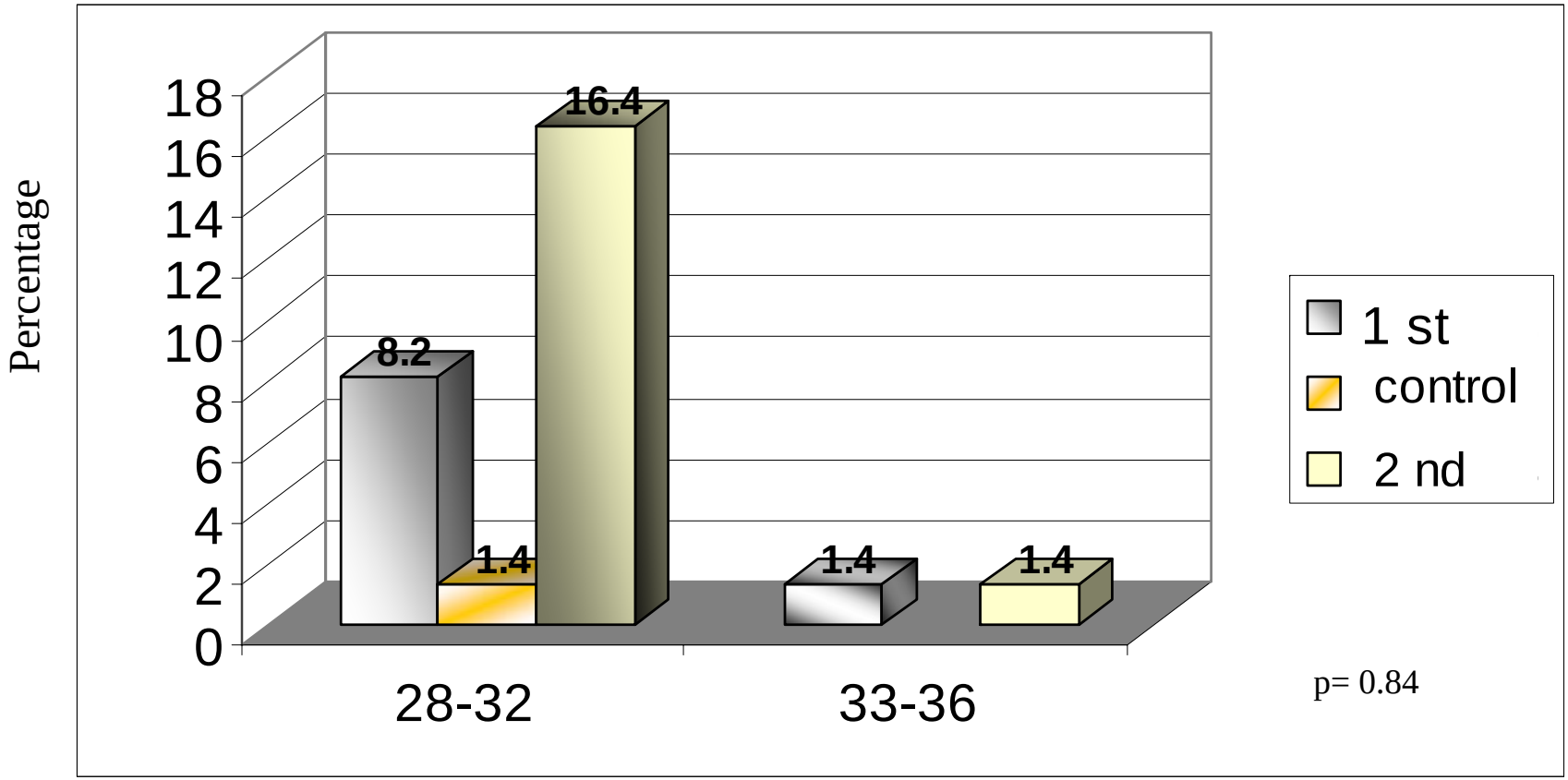


Figure 5 :The percentage of congenital malformations in second - born twins

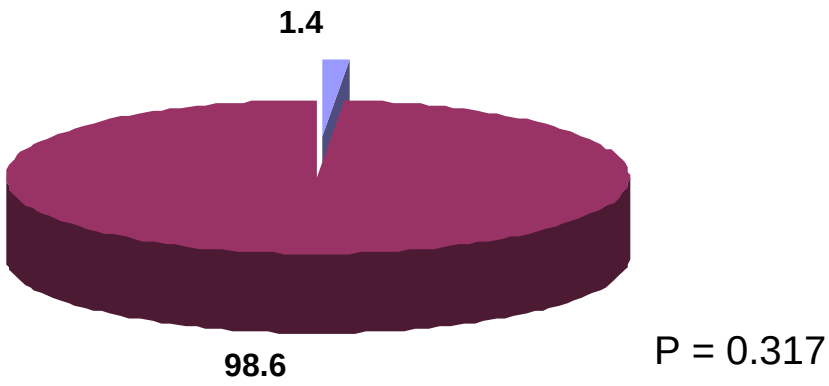


Figure 6 : percentage of family history of multiple pregnancy (case & control)

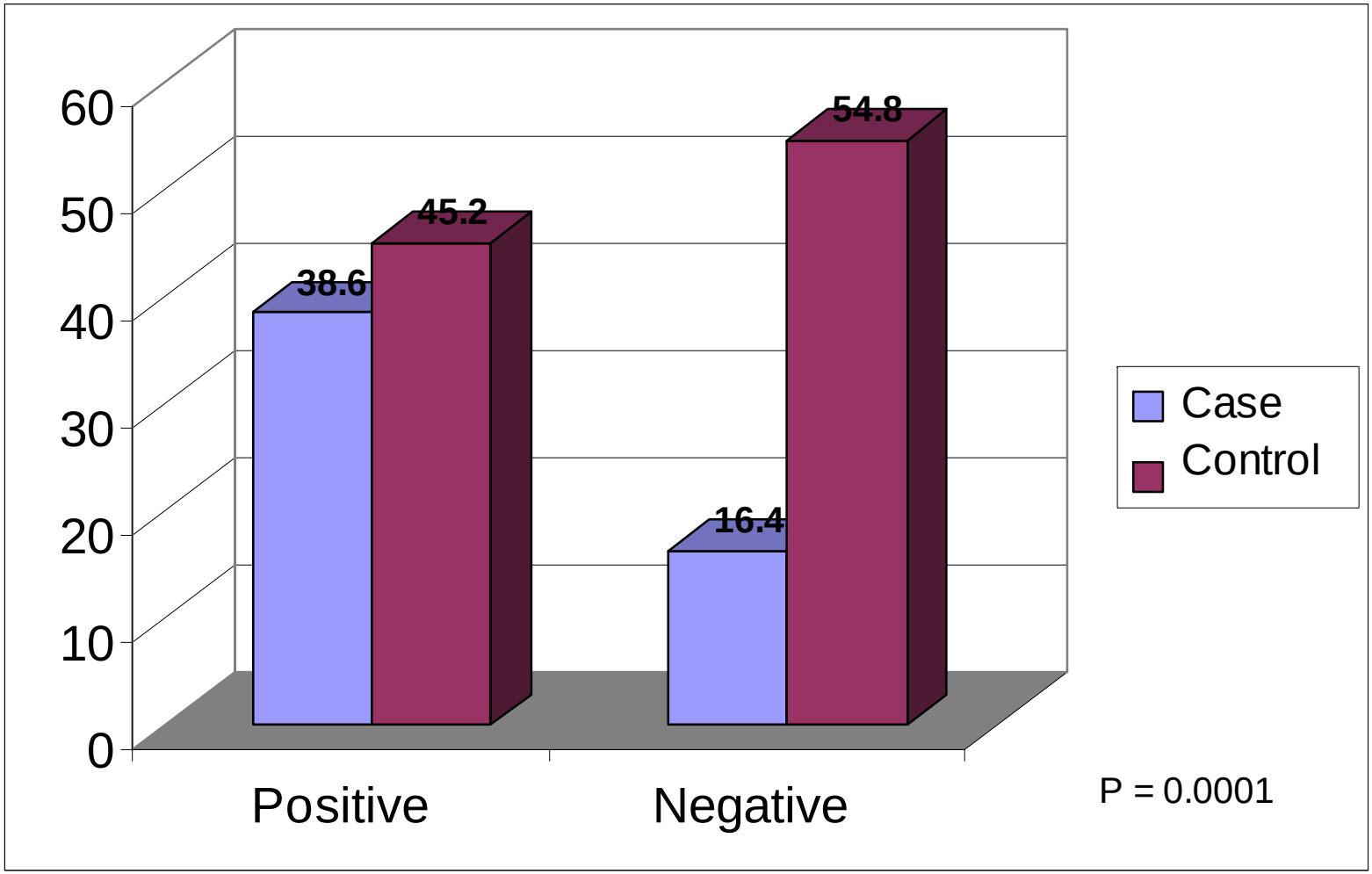


Figure 7 : Percentage of past history of multiple pregnancy (case & control)

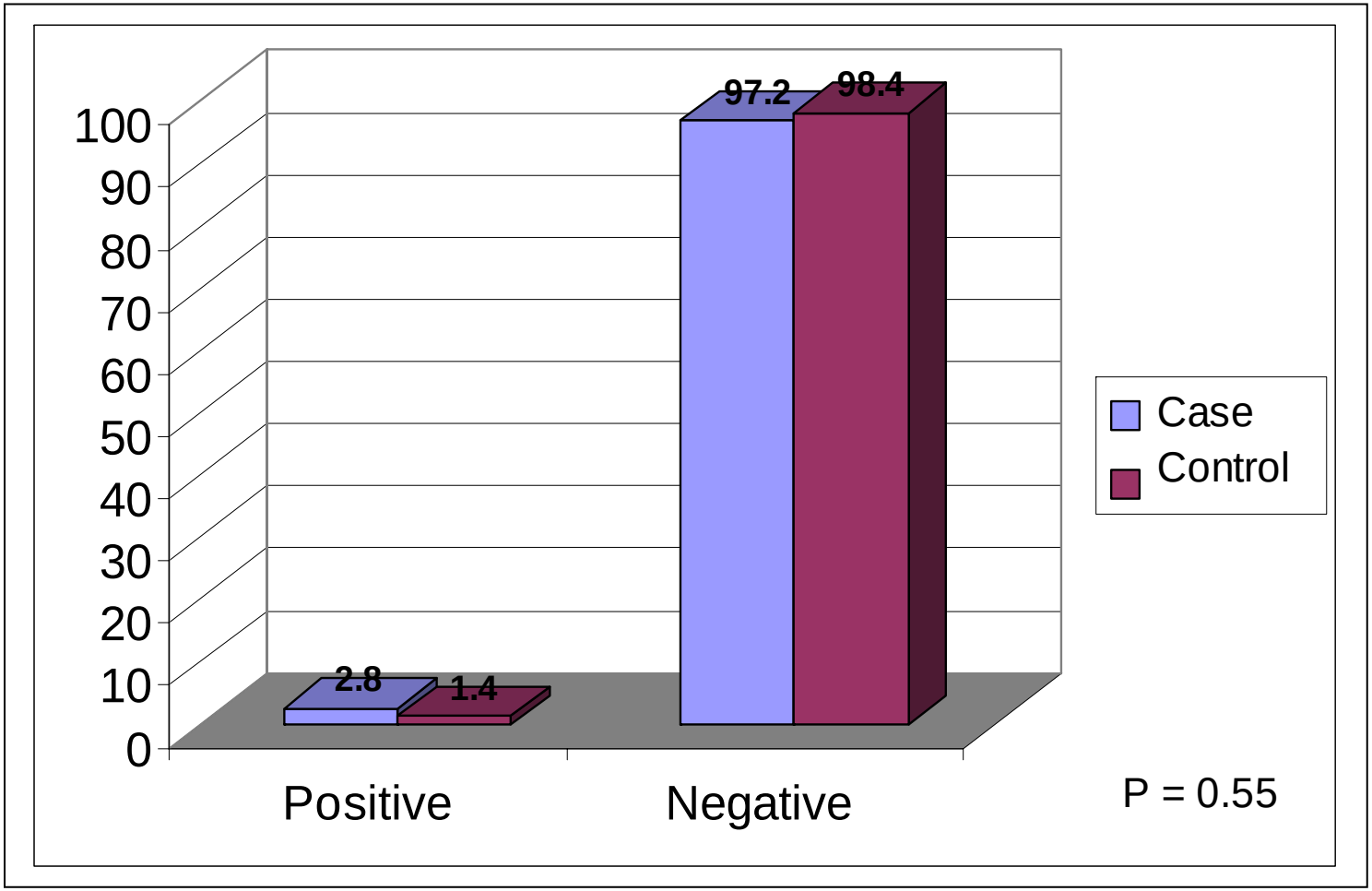


Figure 8: percentage of ovarian stimulant used among control group

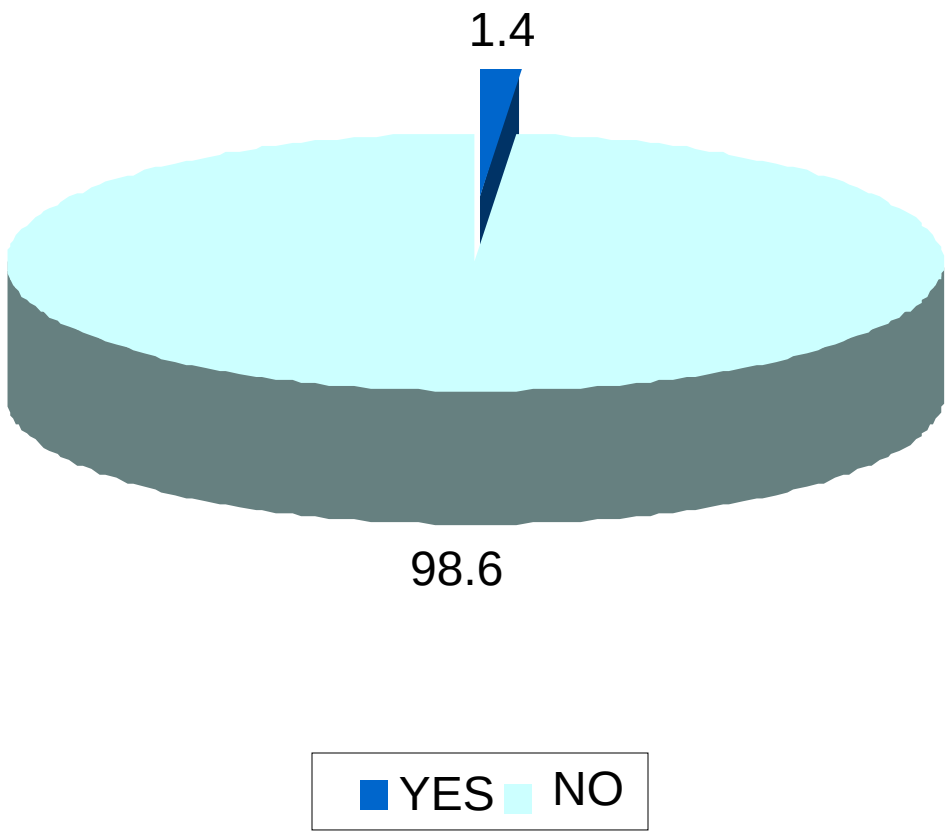
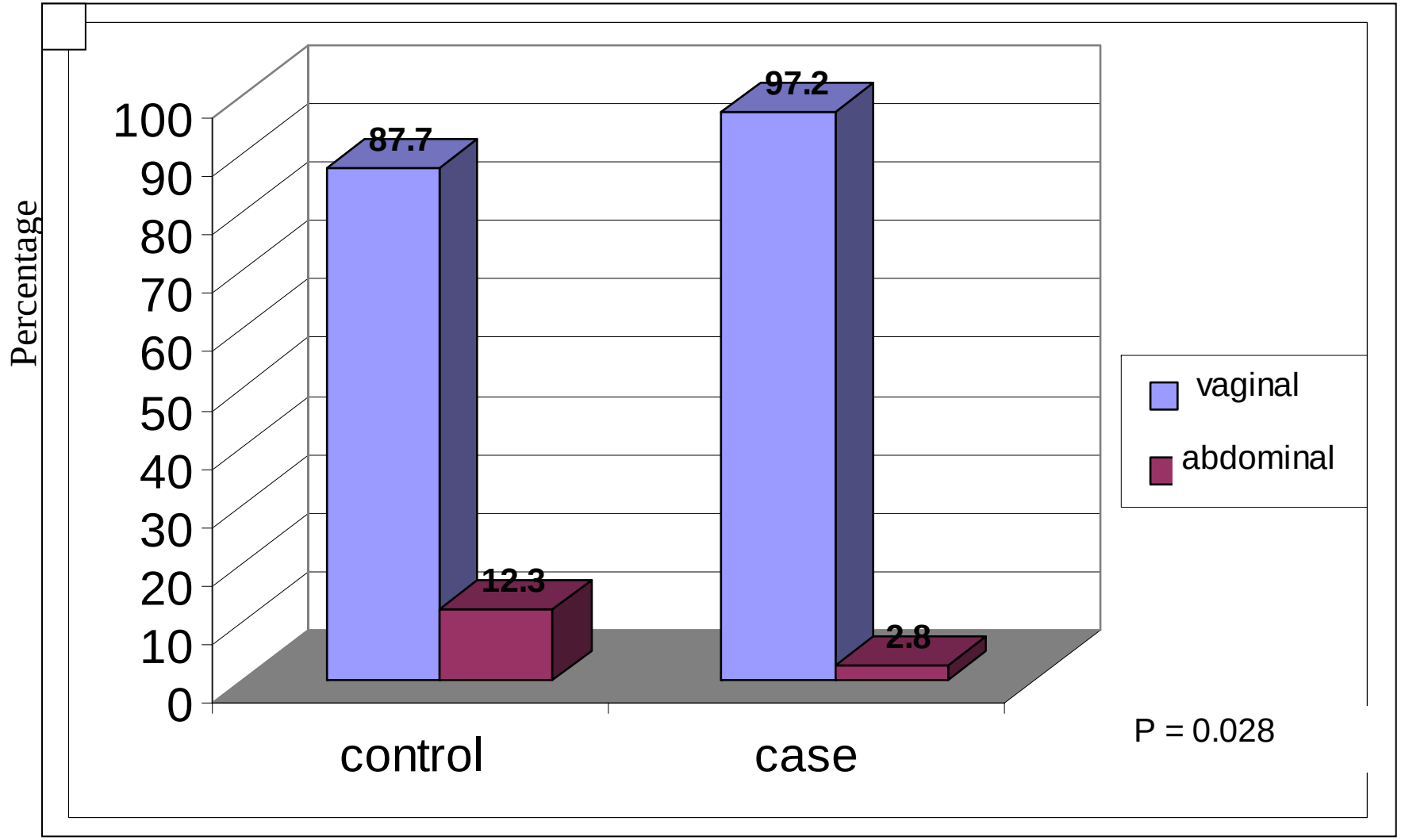


Figure 9 : percentage of mode of delivery (case & control)



University of Khartoum
Faculty of Medicine
Department of paediatrics and child health

Perinatal outcome of multiple-birth new borns in some Hospitals in Khartoum

Serial No: date……hospital……

A) Mother's History

1- Name ……2- Age …… 3-Trible…….....

4- Residence :a) Province ……. b) Town …….

c)Block ……. d) House No …….

e) Telephone No ……...

5- Blood group……. 6- Husband's Name : ……...

7- Drugs (ovarian stimulants) : Yes …….. …. No……..

8- EDD ……. 9- Parity …….

10- PH of multiple pregnancy ……..

11- FH of multiple pregnancy ……..

12- Mode of delivery:

a) Vaginal :

i) Normal ……. ii) Breech …… iii) Ventose …… iv) Forceps ……...

b) Abdominal ……

The indication (s) is (are):

i) Failure of progression ……... ii) Retained 2nd twin(s)……

iii) Malpresention ……. iv) previous scar + multiple gestation

v) G. multiprous + twin(s) vi) contracted pelvis

B) Initial examination of the new born

13- Order of the newborn is

14- Apgar score in :

a) 1 min …… b) 5min…….. c) 10 min ……..

15- Meconium

a) stained …….....b) not stained ……..

16- Resuscitation : a) Yes ……. b) No ……

a) If Yes type of resuscitation :

(i) Tactile stimulation …….. (ii) O2 ……(iii) Ventilation ……...

(iv) Drugs…… Type ……..

b) duration in minutes ……

c) Outcome of resuscitation :

i- Discharged ……..…… ii- Admitted to the nursery ……..

iii- Died ……..

iv- The most likely cause of death ……..

17- If not resuscitated the outcome is :

i) Discharged …… ii) Admitted to postnatal ……

iii) Admitted to NICU ……..

18- Sex : a) male ……. ….b) female ……..

C) detailed examination

19- Gestational age …… wks

20- General : a) pale …….. b) Jaundiced ……. C) Cyanosed…….

d) Anus …….e) Hip…….f) ill……g)well ……

21- Anthropometery : a) Wt ……(kg) – centile …….

b) Length…….(cm) – centile ……..

c) Hc …….(cm) – centile ……..

22- System examination :

i) CNS …….

a) Tone ……..b) Primitive reflexes ……..

c) Others……

ii) CVS : a) HR …….b) S1 …… C) S2……

d) Murmur …….. e) Added sound ……

iii) Respiratory : a) RR……..b) Chest movement ……

c) Breath sound …….d) Added sound ……...

iv) – Abdomen : Organomegally : Yes …… No……...

If yes specify :……

23) Dysmorphic feature : Yes…….. No ……..

If yes specify :…… …

D) Follow –up of the newborn :

* the in-patient :

24- Developed complication (s) Yes…… No…….

i) If yes specify :……

ii) The clinical evidence (s) is (are) ……

……

……

…….

iii) Relevant investigations ……..

……

……

…….

25- The outcome is :

i) Discharged …….. ii) Still in nursery or postnatal after day 7 …….

iii) Died …….. and the most likely cause of death is ……

* The out patients :

26- Alive and well at day 7

27- Died

28- Developed complication (s): Yes…….. No…….

a) If yes (specify):……
……

b) And the clinical evidence is……

c) The relevant investigations……
……

d) The outcome is :……

- Readmitted and still in hospital by day 7…….
- Readmitted and discharge by day 7…….
- Died:…….. the most likely cause of death…….

.